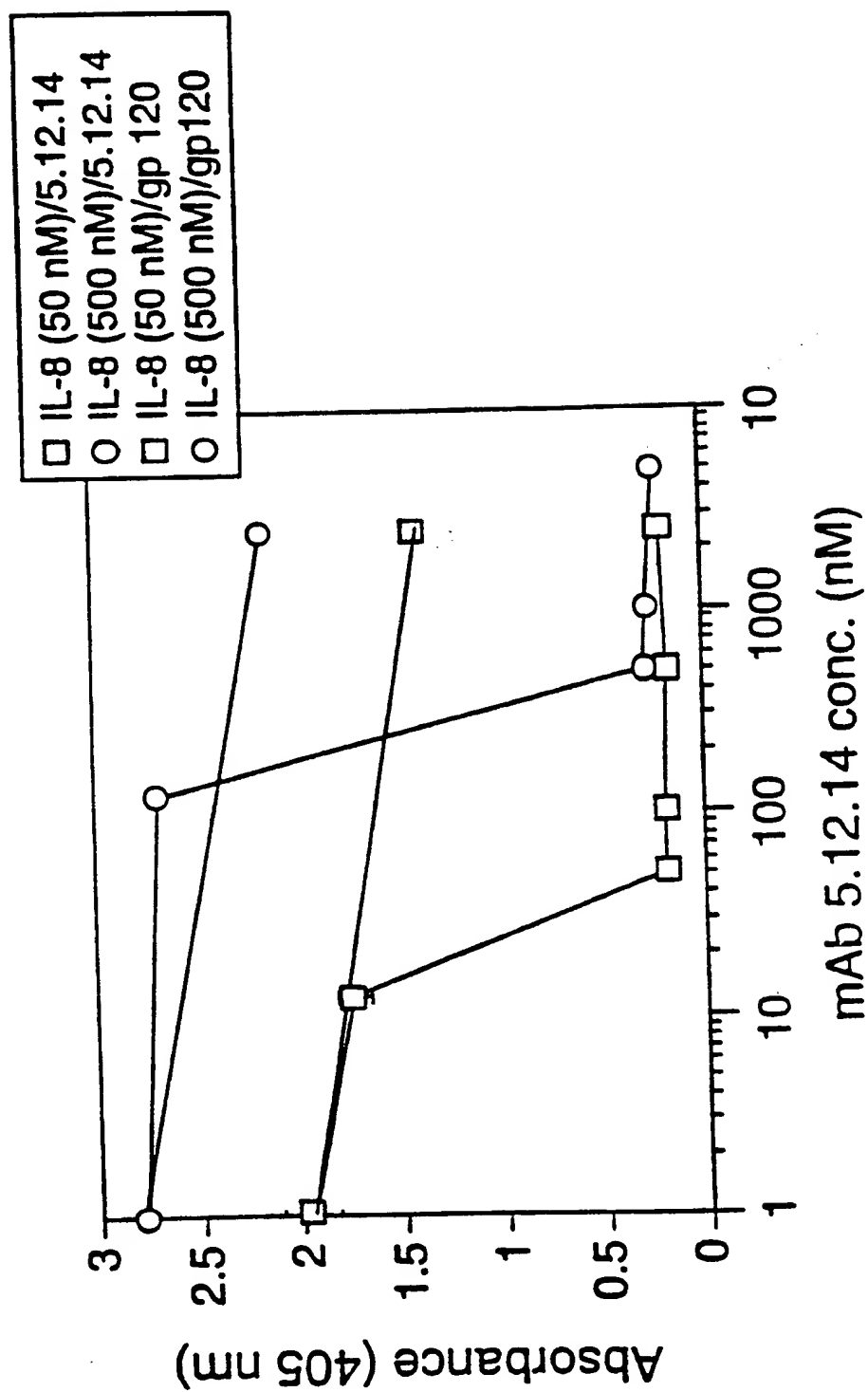
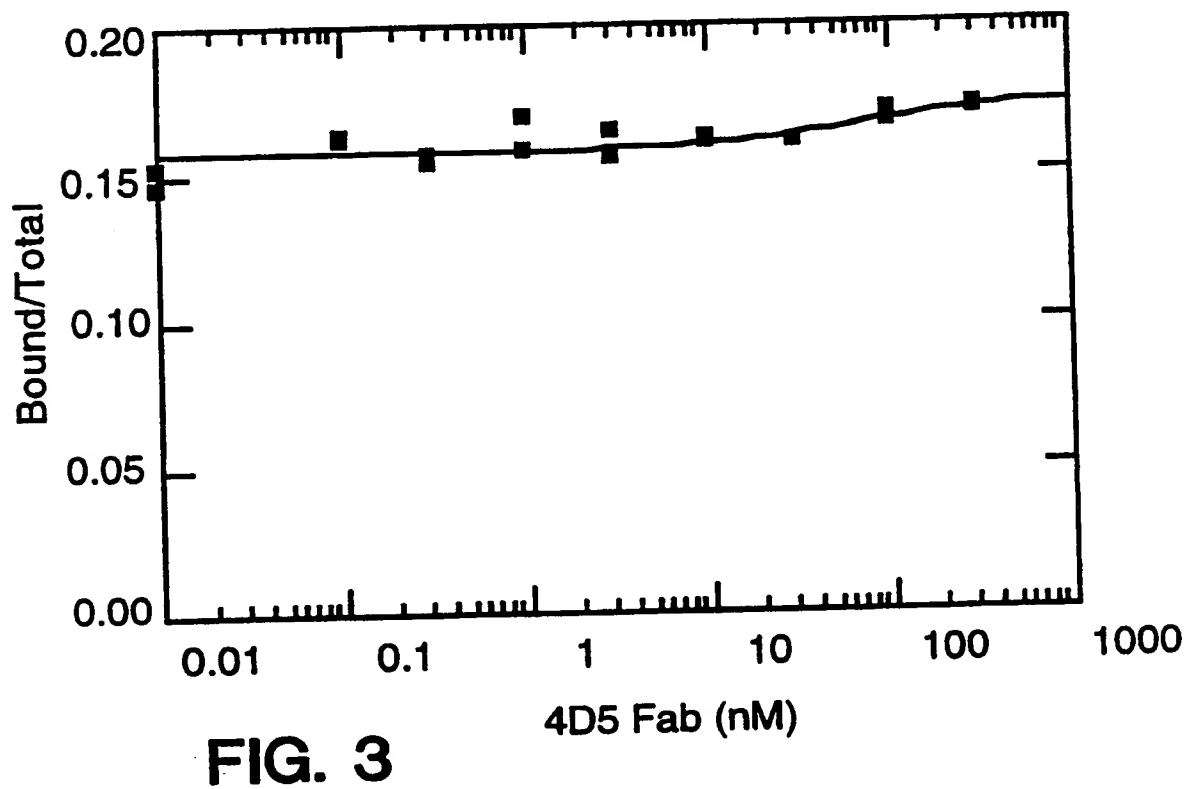
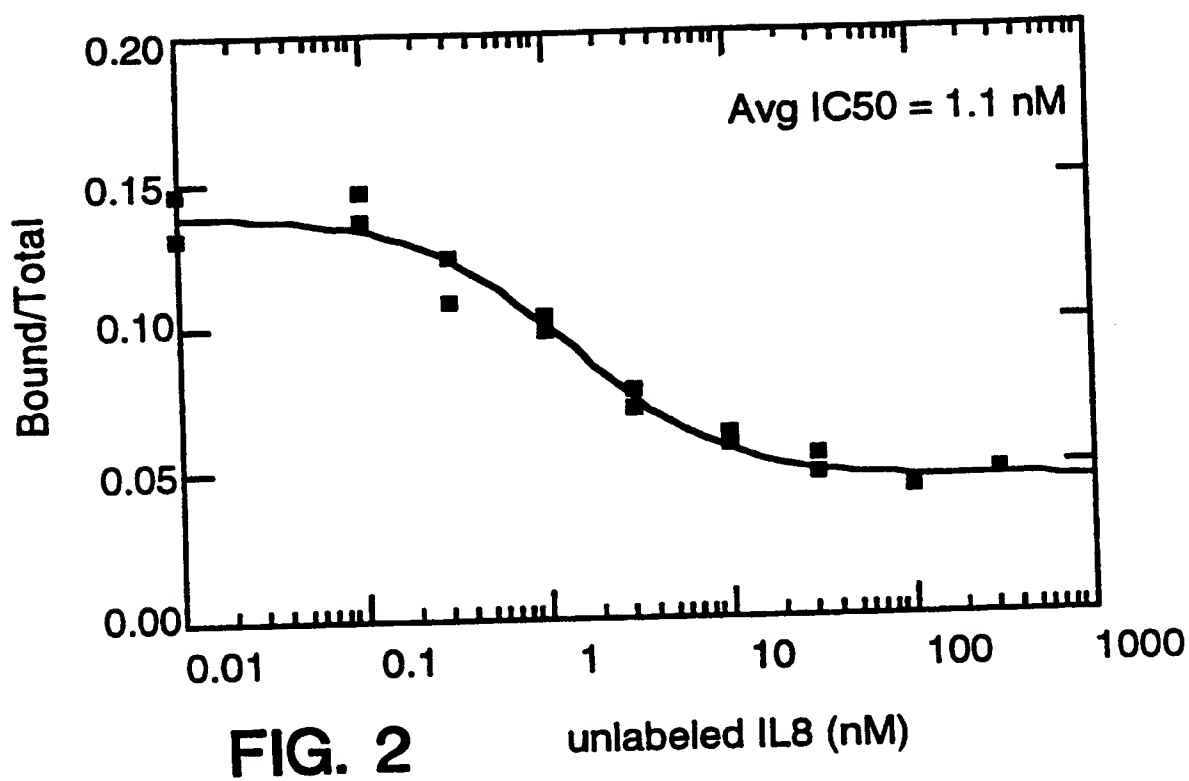


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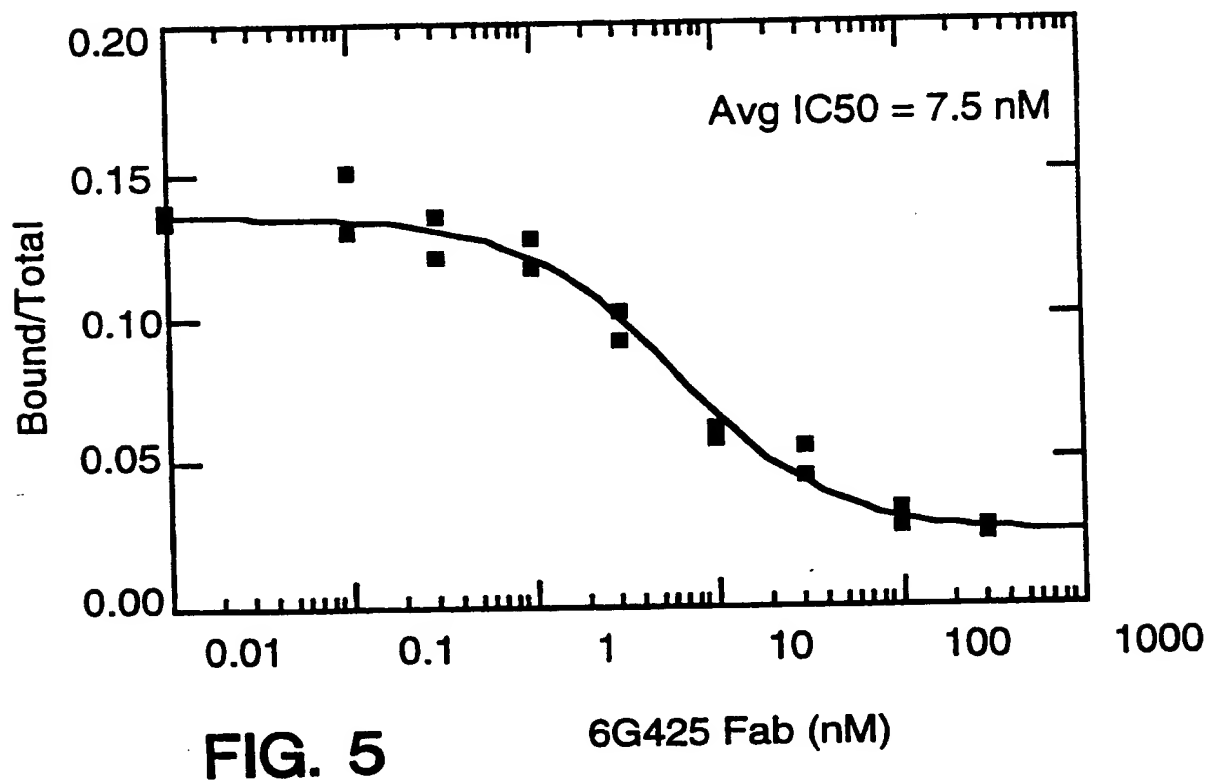
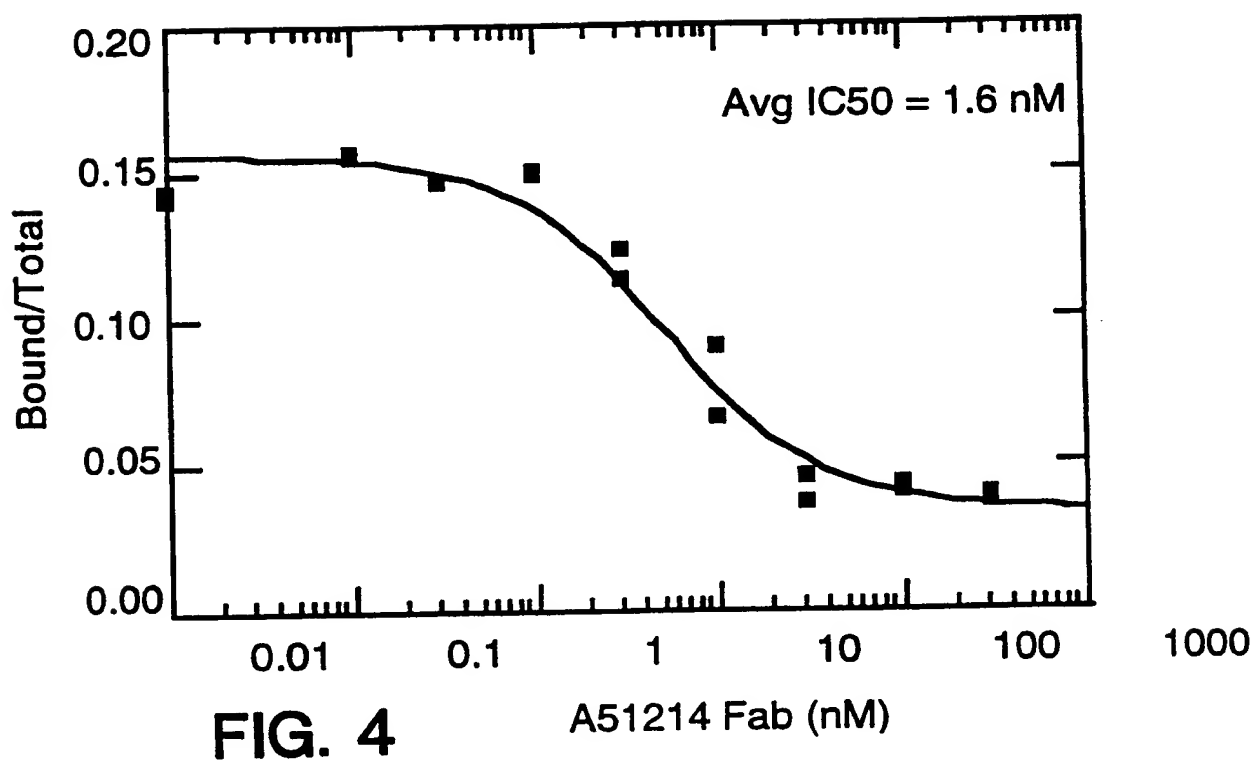
FIG. 1



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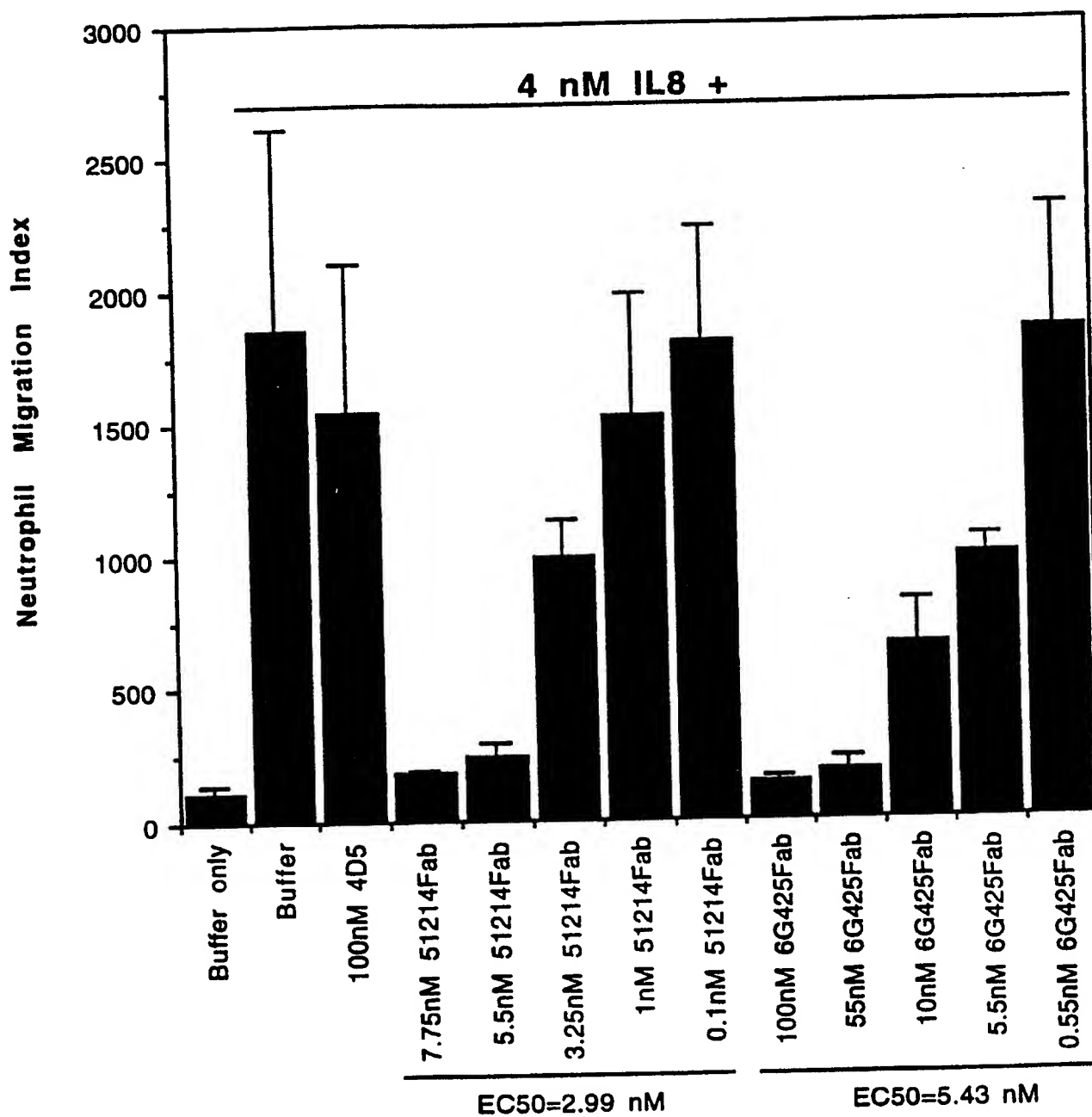


FIG. 6

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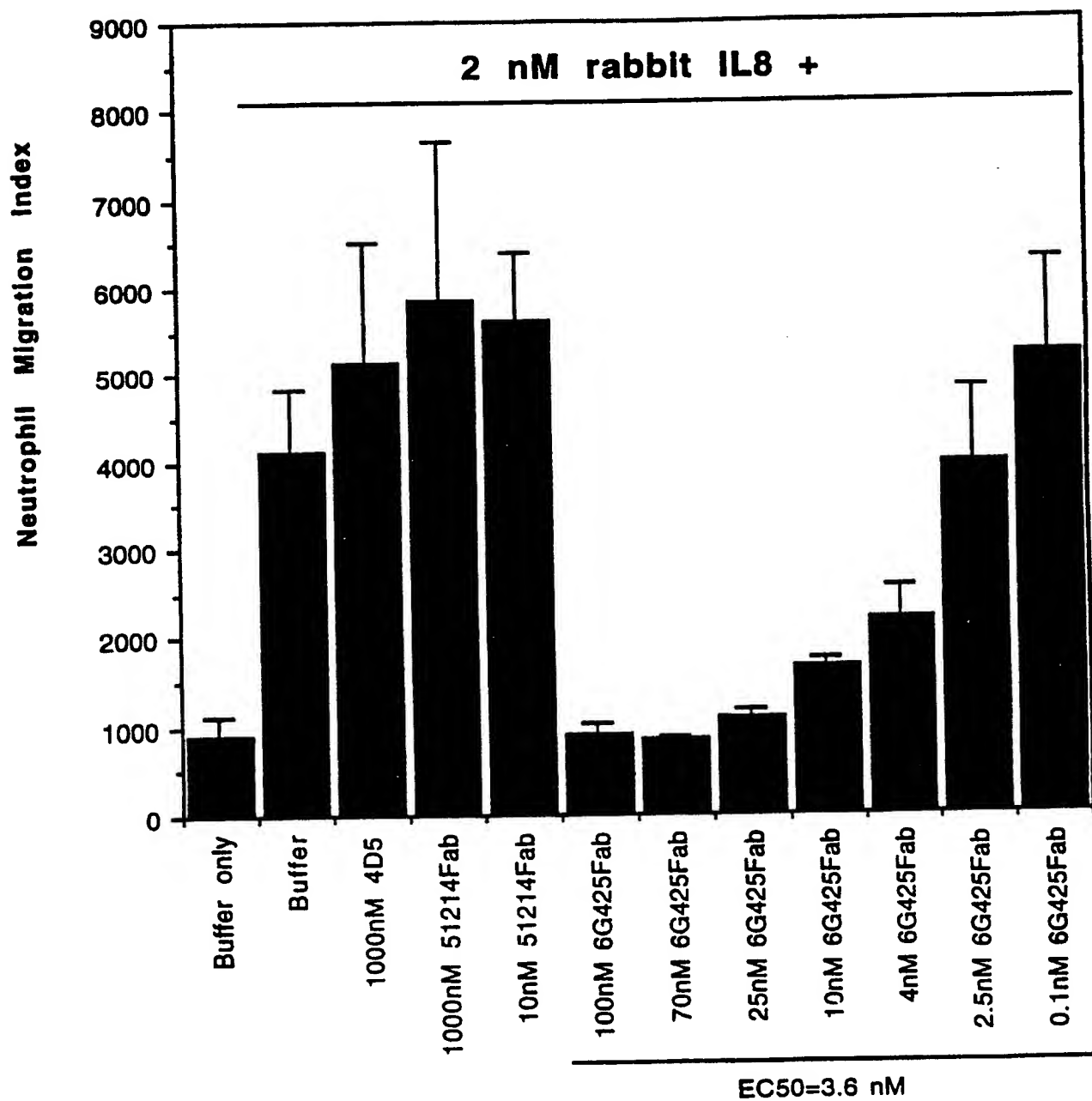
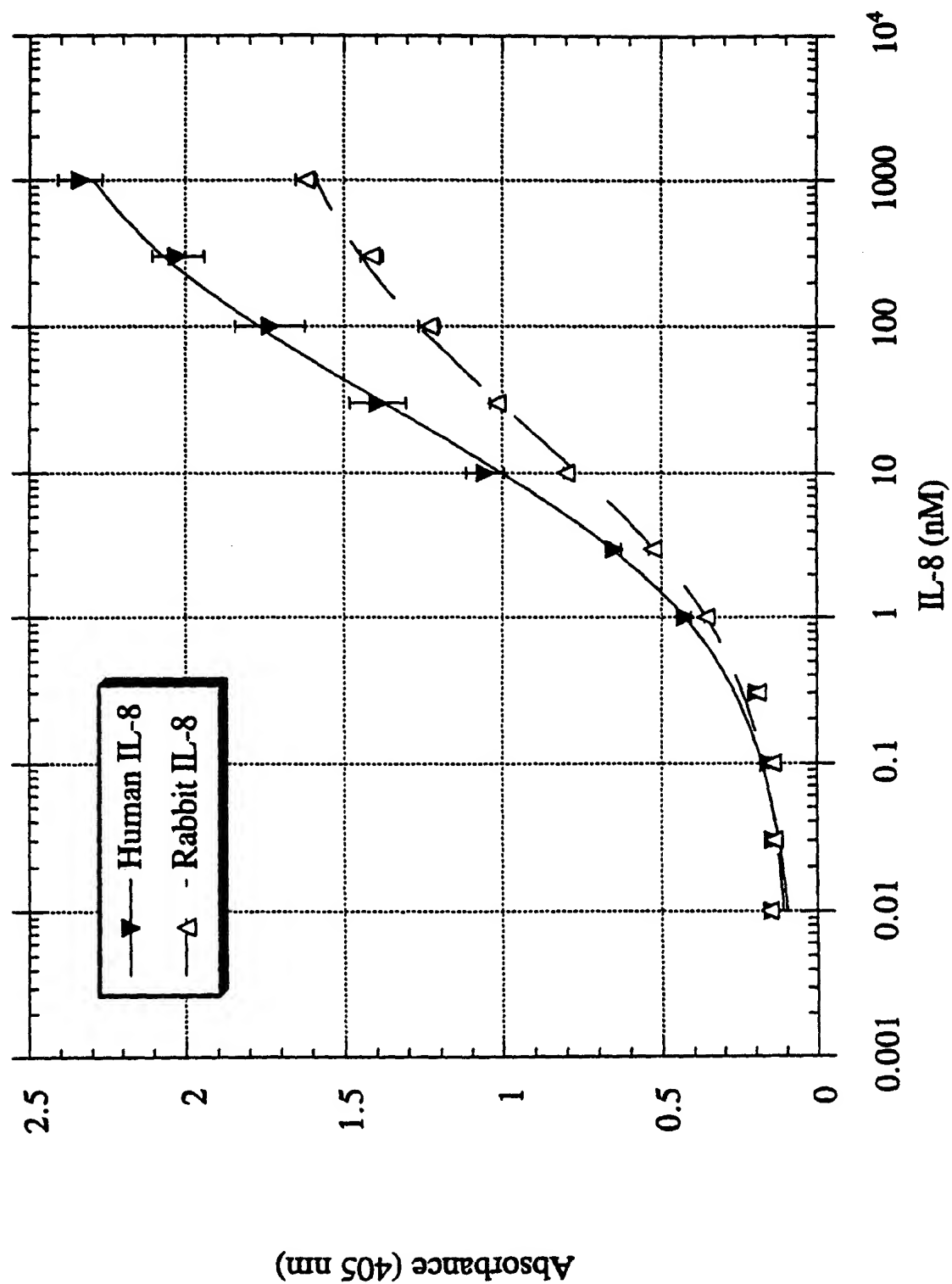


FIG. 7

FIG. 8



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FIG. 9

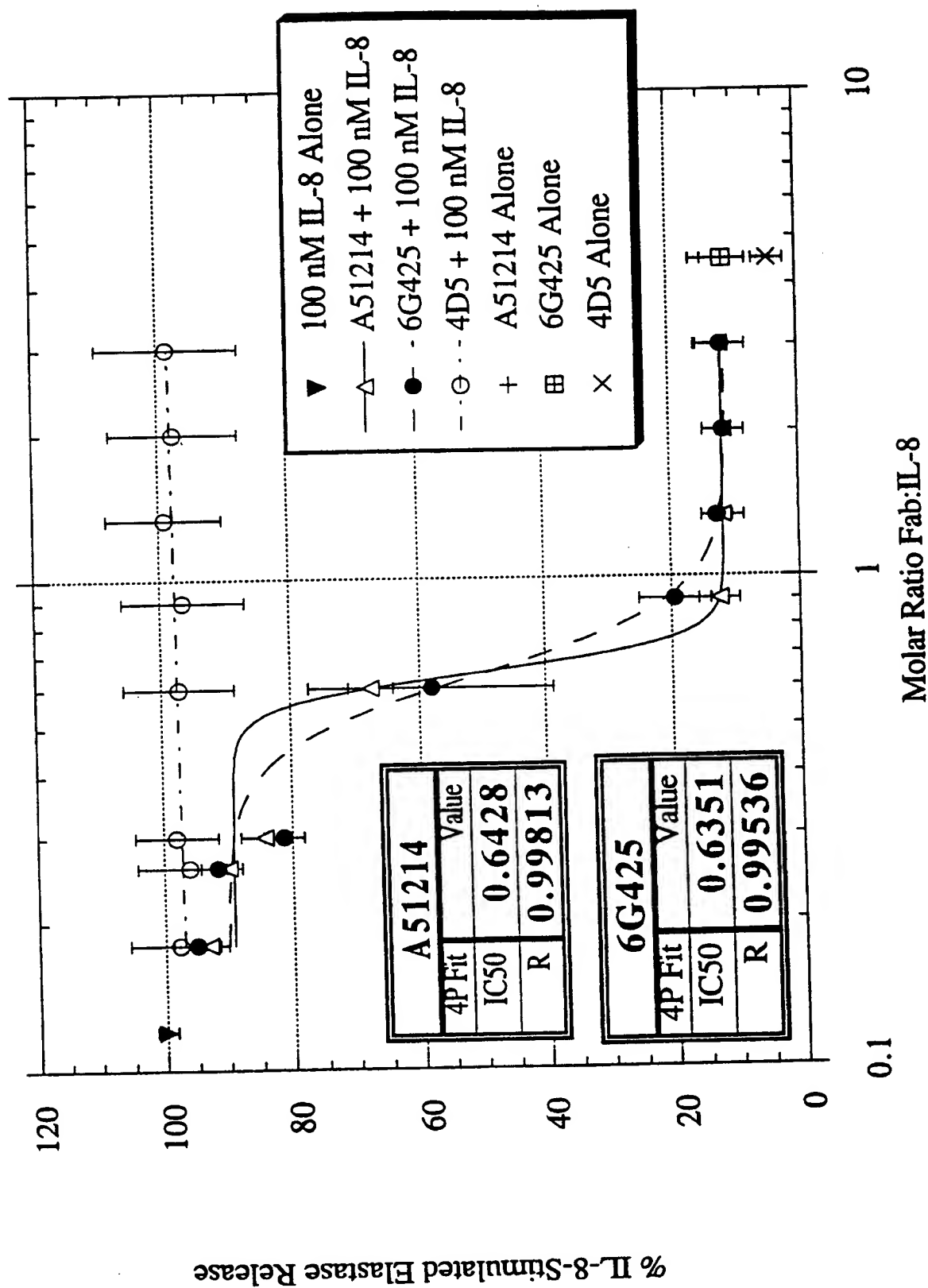
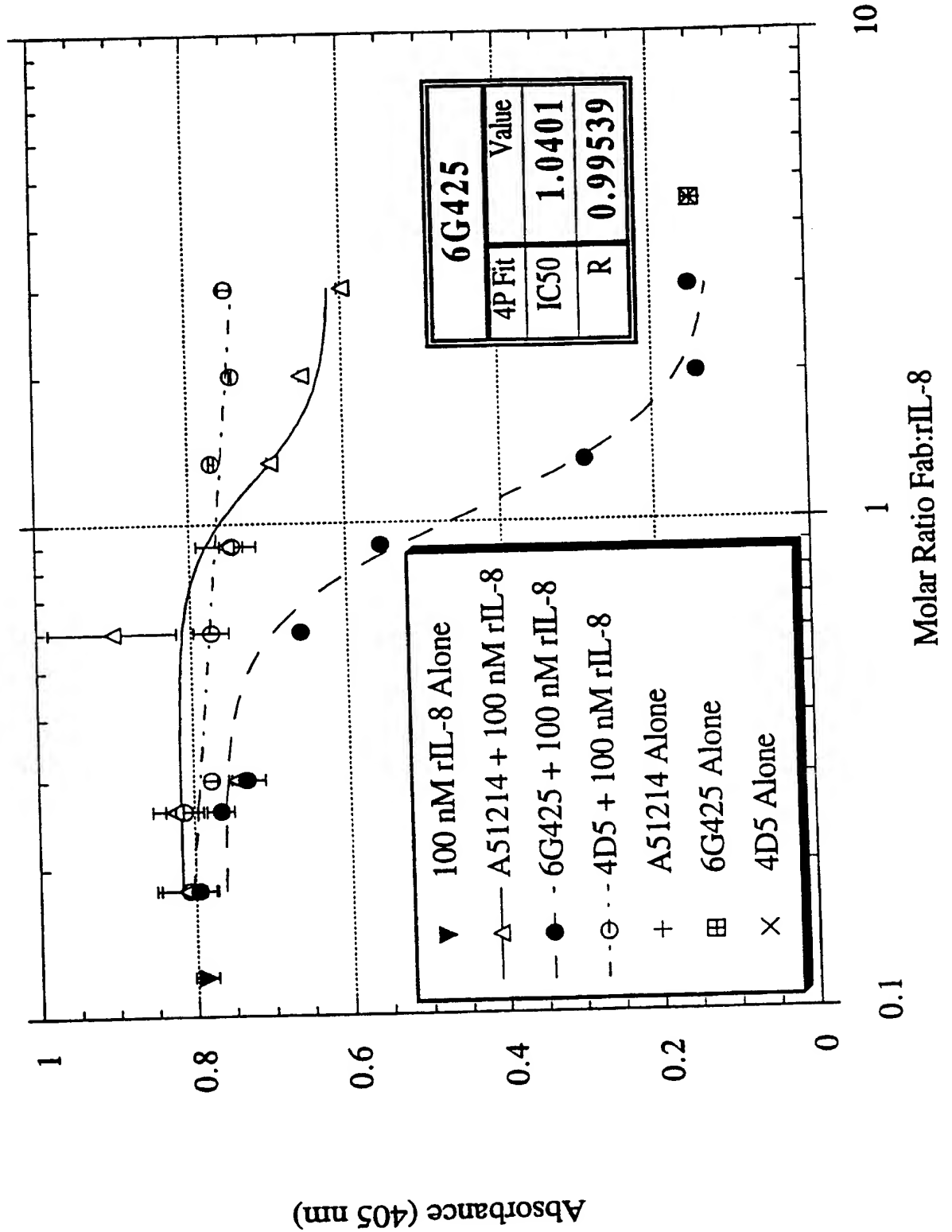


FIG. 10



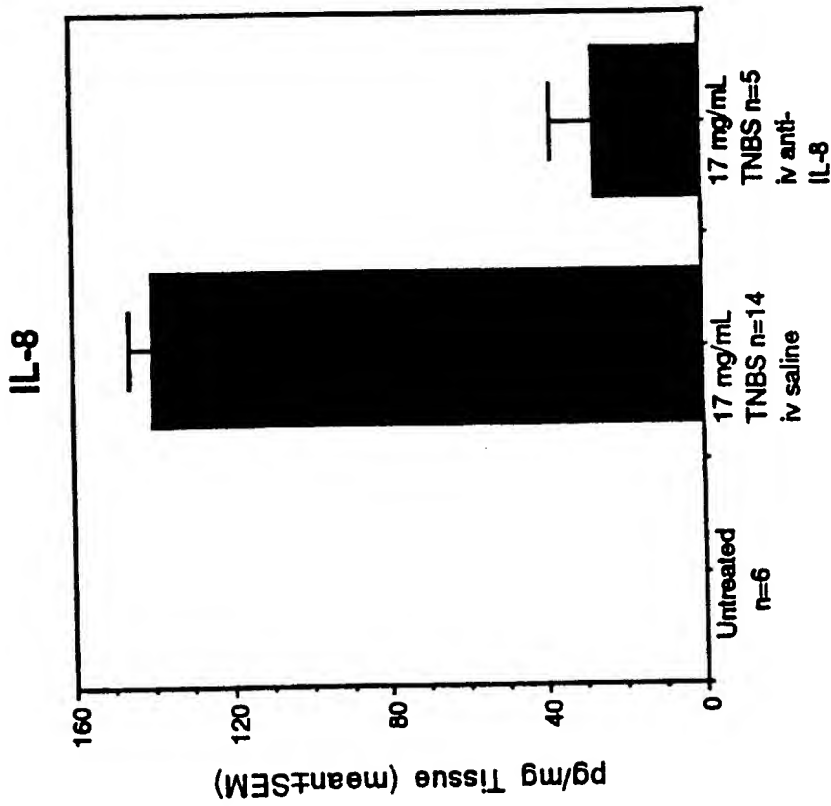


FIG. 11B

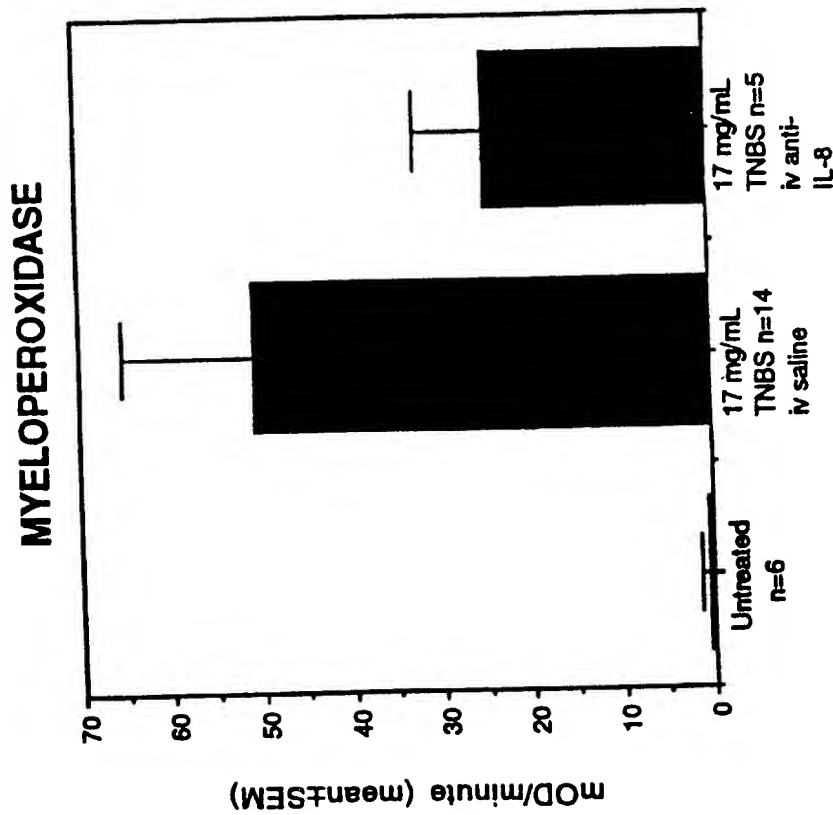


FIG. 11A

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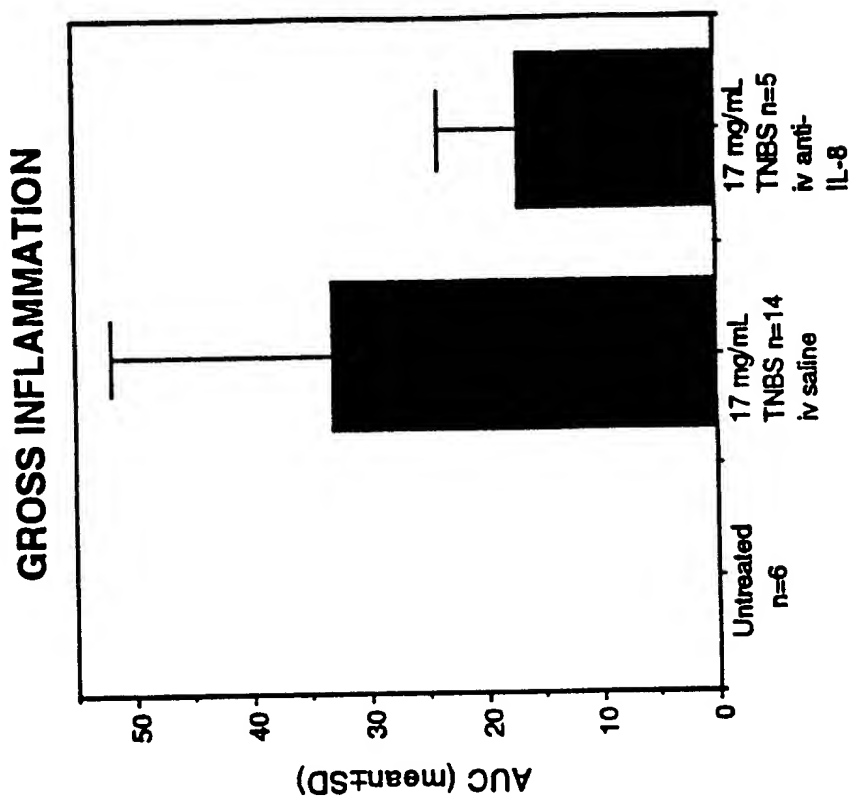


FIG. 11D

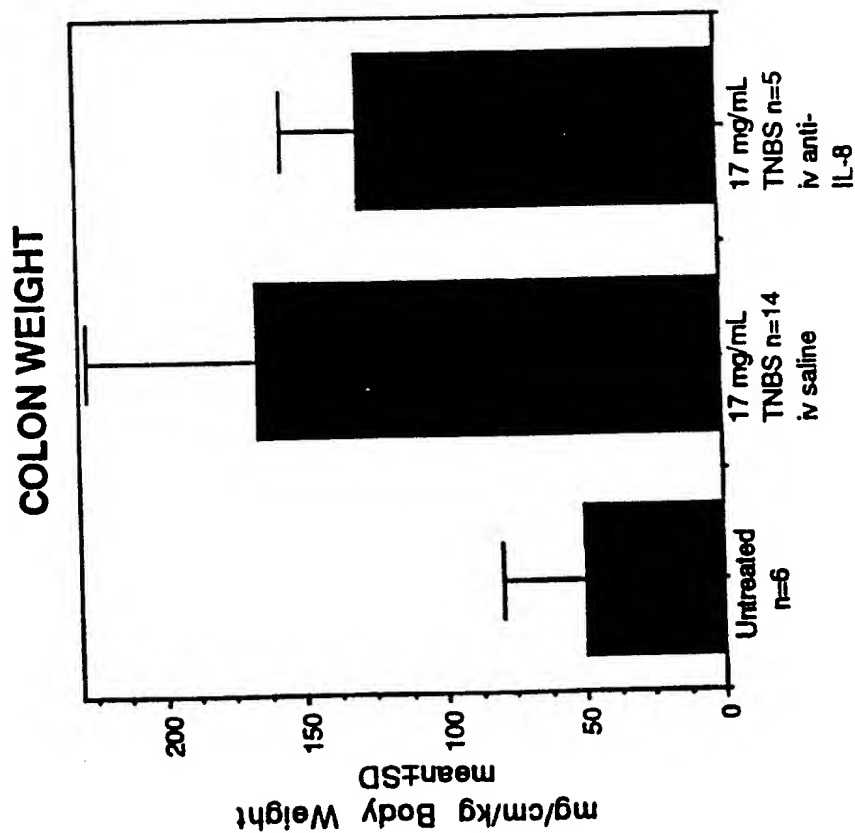


FIG. 11C

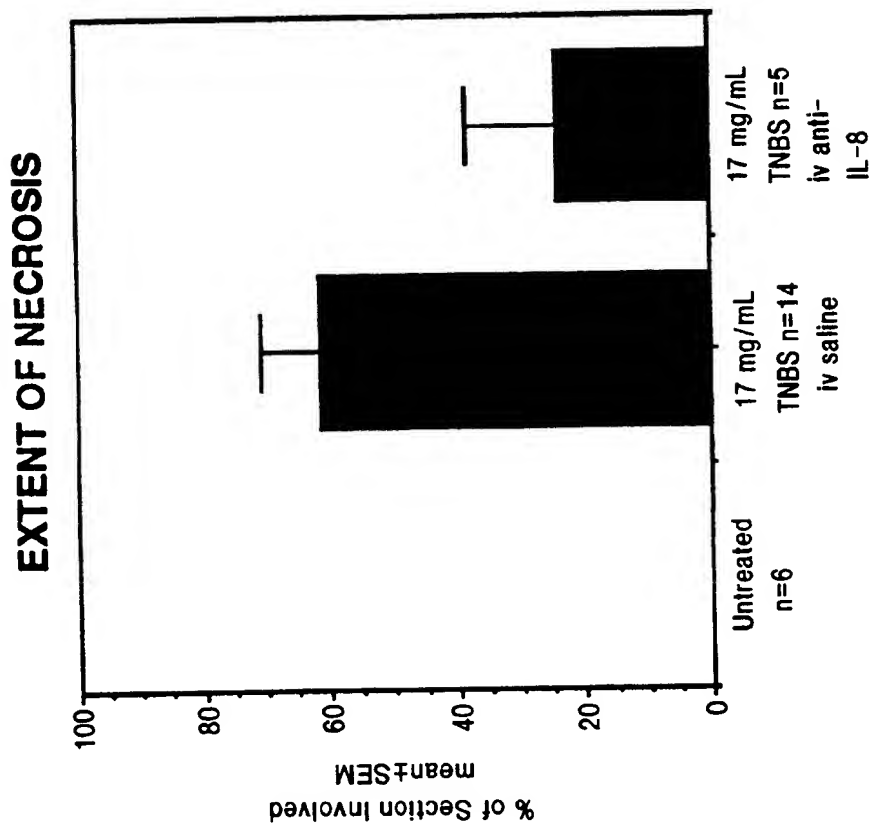


FIG. 11F

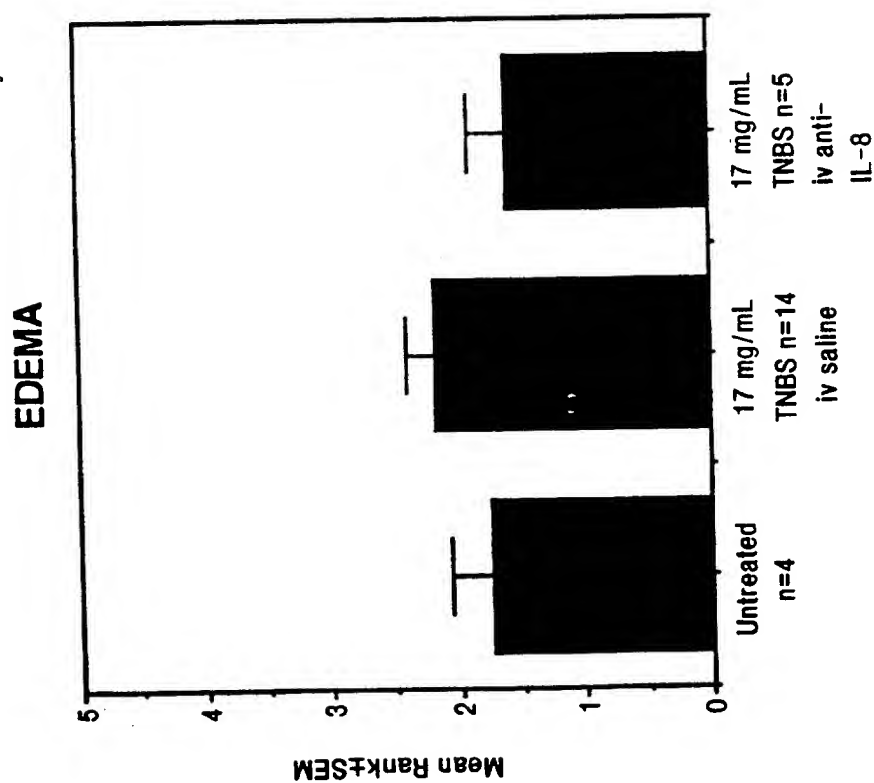


FIG. 11E

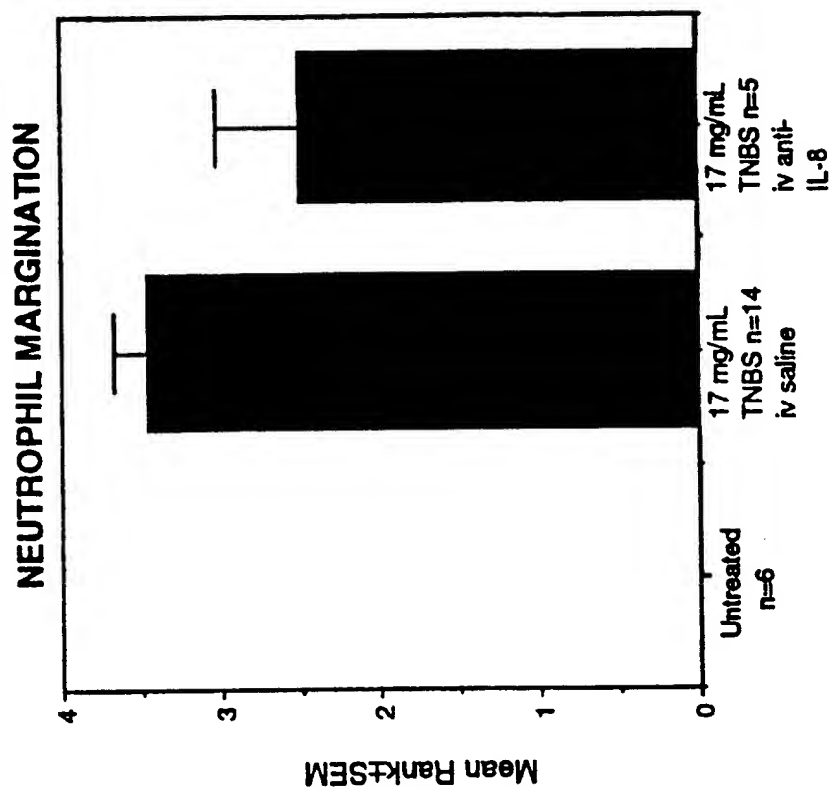


FIG. 11H

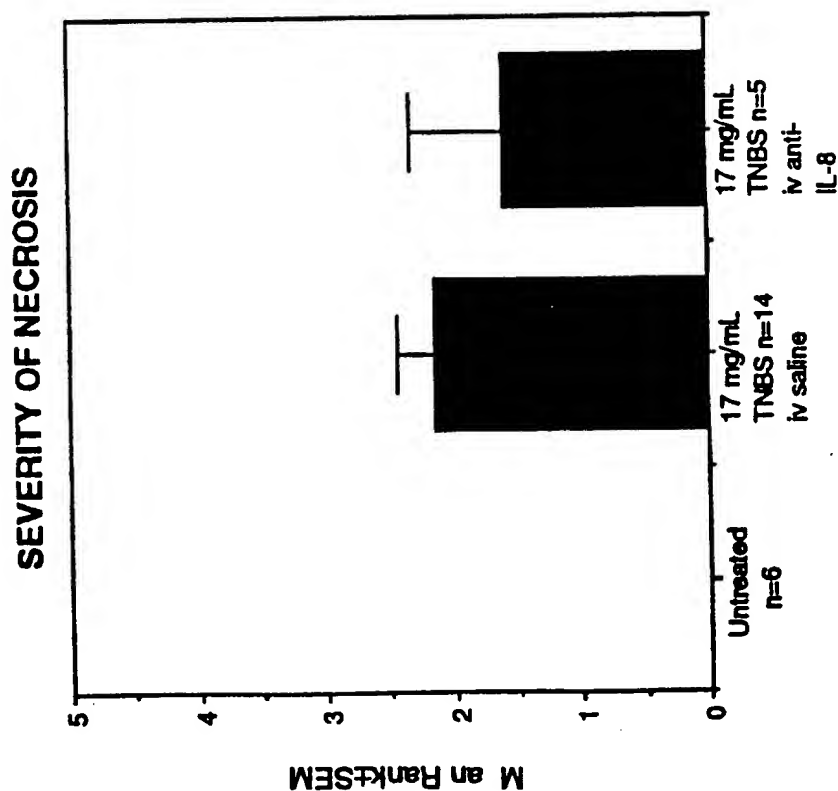


FIG. 11G

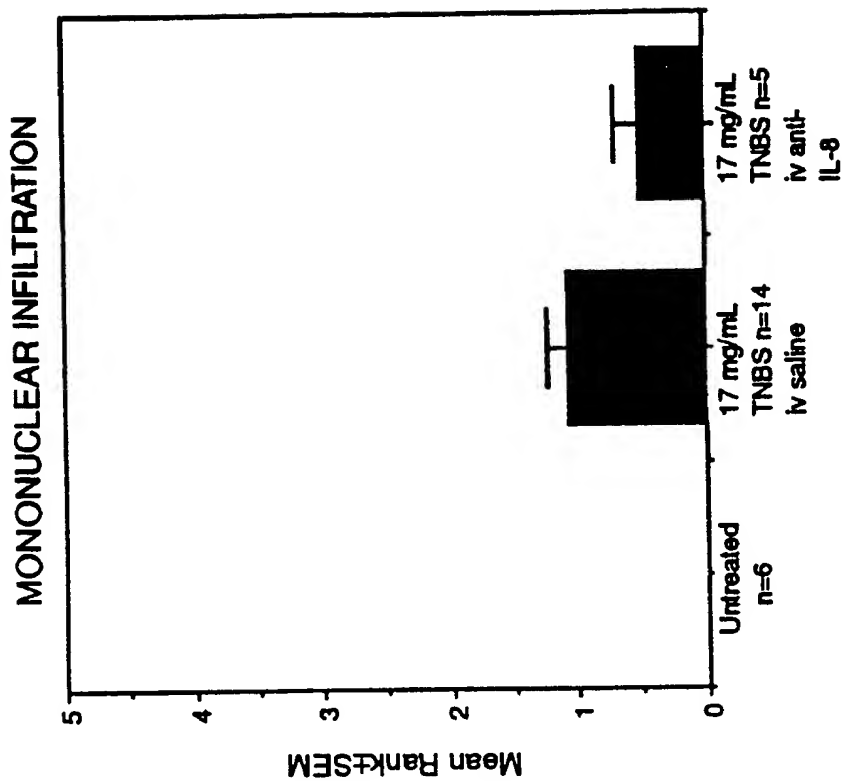


FIG. 11J

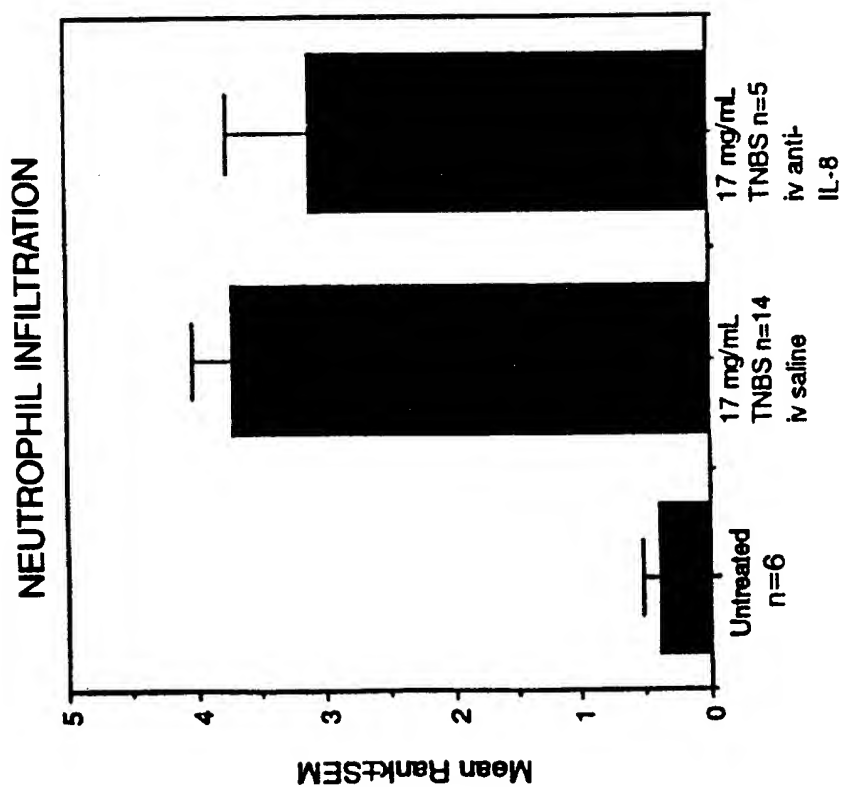
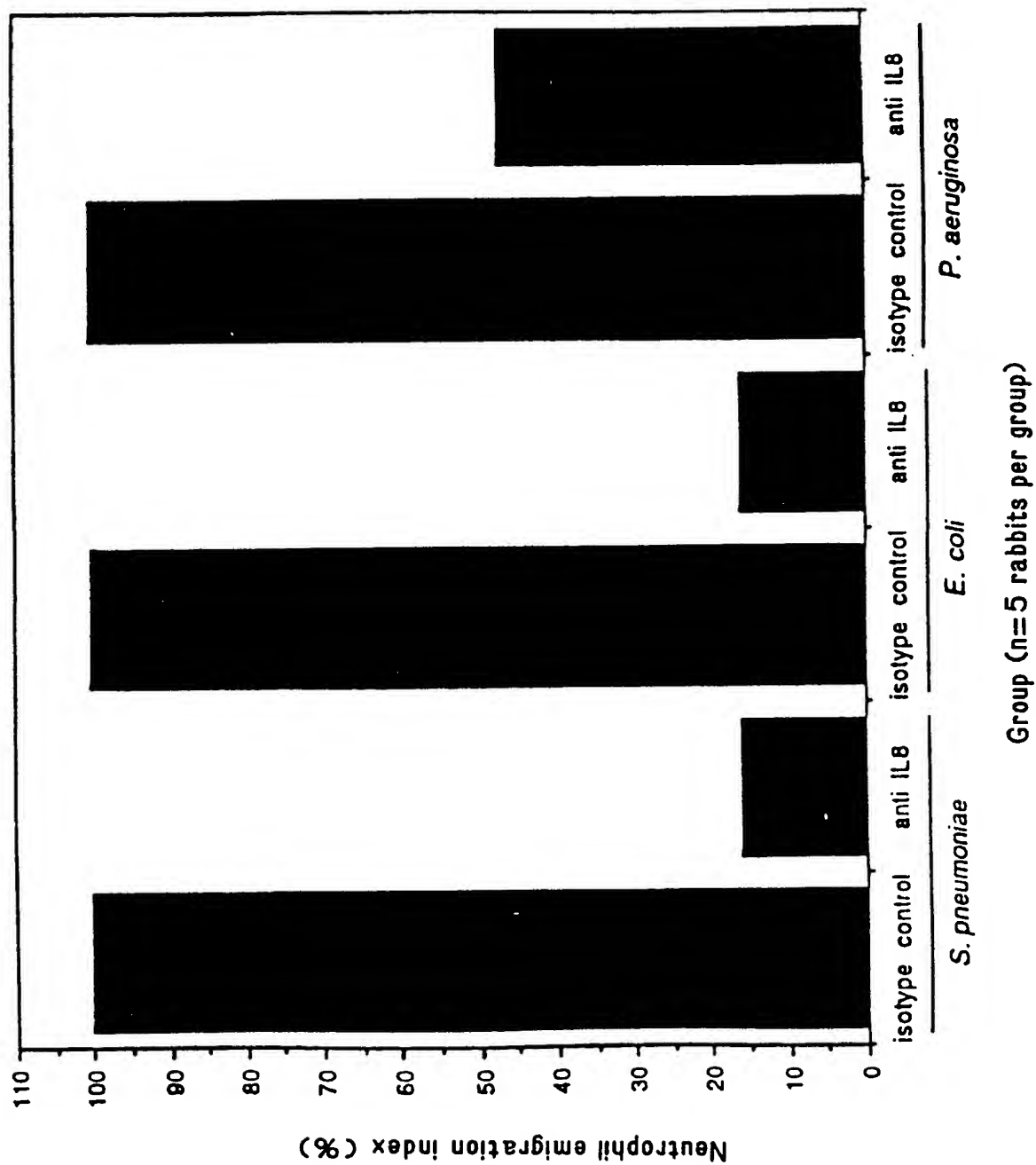


FIG. 11I

FIG. 12



Light Chain Primers:

MKLC-1, 22mer

FIG. 13

5' CAGTCCAACCTGTTTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

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FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC 3'
 T T T
 A

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3'

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Heavy chain forward primer

FIG. 15

SL002B 39 mer

5' CGATGGGCCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T
G
A

C

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCGG ATAGACCGATGGGGCTGTTGTTTTGGC 3'

T
A
G

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1 GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC
CTGTAACAGT ACTGTGTCAG AGTTTTTAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCTTTGGT
21 V T C K A S Q N V G T N V A W Y Q Q K P

CDR #1

121 GGGCAATCTC CTAAAGCACT GATTACTCG TCATCCTACC GGTACAGTGG AGTCCCTGAT
CCC GTTAGAG GATTTCGTGA CTAAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA
41 G Q S P K A L I Y S S Y R Y S G V P D

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGACAGAT TTCACTCTCA CCATCAGCCA TGTGAGTCT
GCGAAGTGTG CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAAGTCGGT ACACGTCAGA
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATTT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCT
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA
81 E D L A D Y F C Q Q Y N I Y P L T F G P

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTTCCA
CCCTGGTTCG ACCTCAACTT TGCCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGT
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTTCGAA
GGTAAGCTT

121 P F E

FIG. 16

1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT
AAGATAACGA TGTTTTCGCA TCGCACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA
1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTCATAT TCAGTAGTTA
CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT
13 P P G G S L K L S C A A S G F I F S S Y
* *

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCG CAACCATTA
ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT
33 G M S W V R Q T P G K S L E L V A T I N
* * *

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG
ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC
53 N N G D S T Y Y P D S V K G R F T I S R
* * * * *

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC
TCTGTTACGG TTCTTGTGGG ACATGGACGT TTACTCGTCA GACTTCAGAC TCCTGTGTGCG
73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA
GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT
93 M F Y C A R A L I S S A T W F G Y W G Q
* * * * *

CDR #3

361 AGGGACTCTG GTCAGTGTCT CTGCAGCCAA AACAAACAGCC CCATCTGTCT
TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCGG GGTAACAGCA
113 G T L V T V S A A K T T A P S V Y

411 **ApaI**
ATCCGGG
TAGGCCC
130 P

FIG. 17

FIG. 18

VL.front 31-MER

5' ACAAAACGCGTACGCTGATATCGTCATGACAG 3'

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3'

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3'

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3'

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1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCTG TTTTCTCTAT TGCTACAAAC
 TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC
 CGCATGCGAC TATAGCAGTA CTGTGTCAGA GTTTTTTAAGT ACAGGTGTAG TCATCCTCTG
 -3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA
 TCCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT
 18 R V S V T C K A S Q N V G T N V A W Y Q
 * * * * * * * * * * * * * *

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA
 GTCTTTGGTC CCGTTAGAGG ATTTCTGTGAC TAAATGAGCA GTAGGATGGC CATGTCACTT
 38 Q K P G Q S P K A L I Y S S S Y R Y S G
 * * * * * * * * * *

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT
 CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA
 58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTCAGCAAT ATAACATCTA TCCTCTCACG
 CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC
 78 V Q S E D L A D Y F C Q Q Y N I Y P L T
 * * * * * * * * * *

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC
 AAGCCAGGAC CCTGGTTTGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG
 98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTGTCT CTGTTGTGTG CCTGCTGAAT
 AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA
 118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT
 TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA
 138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTCAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC
 TTGAGGGTCC TCTCACAGTG TCTCGTCCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTCG
 158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC
 TGGGACTGCG ACTCGTTTTC TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG
 178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG
 GTAGTCCCGG ACTCGAGCGG GCAGTGTTC TCGAAGTTGT CCCCTCTCAC
 198 H Q G L S S P V T K S F N R G E C

711 TTAA
 AATT

216 O

FIG. 19

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1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC
 CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCTCCGA ATCACGGCGG ACCTCCCAGG
 -3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTC ATATTCAGTA GTTATGGCAT GTCTTGGGTT
 GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA
 18 L K L S C A A S G F I F S S Y G M S W V
 * * * *

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC
 GCGGTCTGAG GTCCGTTCTC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG
 38 R Q T P G K S L E L V A T I N N N G D S
 * * * *

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC
 TGGATAATAG GTCTGTCACA CTTCCTCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG
 58 T Y Y P D S V K G R F T I S R D N A K N
 * * * *

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTACTGTGCA
 TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT
 78 T L Y L Q M S S L K S E D T A M F Y C A

361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTACTGCGG GCCAAGGGAC TCTGGTCACT
 TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAGTGA
 98 R A L I S S A T W F G Y W G Q G T L V T
 * * * *

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC
 CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG
 118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG
 TGGAGACCCC CGTGTGCGCCG GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC
 138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAACCTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCTA
 TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT
 158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC
 GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG
 178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

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661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA
TGGGTCTGGA TGTAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT
198 T Q T Y I C N V N H K P S N T K V D K K
721 GTTGAGCCCA AATCTTGTGA CAAAACACAC ACATGA
CAACTCGGGT TTAGAACACT GTTTGTAGTG TGTACT
218 V E P K S C D K T H T O

FIG. 20B

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Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAAC TGTTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

FIG. 21

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Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3'
 T T T T
 A A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'

FIG. 22

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Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3'
 T C

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3'
 T
 A
 G

FIG. 23

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70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGAGAT
 C TATAGACTA CTGTGTCTGT GGTGAGAGG ACGGACAGTC AGAACCTCTA
 1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGTCAG ATCTAGTCAG AGCCTTGTCAC ACGGTATTGG AAACACCTAT
 GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
 18 Q A S I S C R S S O S L V H G I G N T Y
 * * * * * * * * * * * * * *

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
 AATGTAACCA TGGACGTCTT CCGTCCGGTC AGAGGTTTTCG AGGACTAGAT GTTTCAAAGG
 38 L H W Y L Q K P G Q S P K L L I Y K V S
 * * * * * * * * * *

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTACA
 TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
 58 N R F S G V P D R F S G S G S G T D F T
 * * * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
 GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
 78 L R I S R V E A E D L G L Y F C S Q S T
 * * * * *

CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA
 GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCCG ACTACGACGT
 98 H V P L T F G A G T K L E L K R A D A A
 * * * * *

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA
 GGTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTTAACT
 118 P T V S I F P P S S E Q L K

FIG. 24

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70 G AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
 C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
 1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTCAGTA GCCACTACAT GCACTGGGTG
 CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
 18 V K I S C K A S G Y S F S S H Y M H W V
 * * * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
 TTCGTCTCGG TACCTTTCTC GGAAGTACC TAACCGATGT AACTAGGAAG GTTACCACTT
 38 K Q S H G K S L E W I G Y I D P S N G E
 * * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
 TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAGT GACATCTGTG TAGAAGGTGC
 58 T T Y N Q K F K G K A T L T V D T S S S
 * * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
 TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
 78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
 TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
 98 R G D Y R Y N G D W F F D V W G A G T T
 * * * * *

CDR #3

BstEII ApaI
 421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGCC
 CAGTGGCAGA GGAGGCGGAT TTGGCTGTCT GGGTAGCCAG ATAGGCCCGG
 118 V T V S S A K T D S P I G L S G P

471 CATC
 GTAG
 135 I

FIG. 25

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5' CTTGGTGGAGGCGGAGGAGACG 3'

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3'

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3'

FIG. 26

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1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAT
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTA
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT
CGTATGCGAC TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA
-3 A Y A D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCA G ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA
18 Q A S I S C R S S O S L V H G I G N T Y

* * * * *
CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC
AATGTAACCA TGGACGTCTT CGGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG
38 L H W Y L Q K P G Q S P K L L I Y K V S

* * *
CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTACA
TTGGCTAAAA GACCCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT
58 N R F S G V P D R F S G S G S G T D F T
* * * *

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT
78 L R I S R V E A E D L G L Y F C S Q S T

* * * *
CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTGCTGCA
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCC ACAACGACGT
98 H V P L T F G A G T K L E L K R A V A A
* * * * *

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT
GGTTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTTAAC TTAGACCTTG ACGGAGACAA
118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

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661 GCCTGCCAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGCAGT GTTCTCGAA GTTGTCCTCCT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA
CTCACAATT
218 E C O

FIG. 27B

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1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA
 CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT
 -3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG
 CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC
 18 V K I S C K A S G Y S F S S H Y M H W V
 * * * *

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA
 TTCGTCTCGG TACCTTTCTC GGAACTCACC TAACCGATGT AACTAGGAAG GTTACCACTT
 38 K Q S H G K S L E W I G Y I D P S N G E
 * * * * *

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC
 TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAC TACATCTGTG TAGAAGGTCTG
 58 T T Y N Q K F K G K A T L T V D T S S S
 * * * * *

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA
 TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT
 78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG
 TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC
 98 R G D Y R Y N G D W F F D V W G A G T T
 * * * * *

CDR #3

421 GTCACCGTCT CCTCCGCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC
 CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG
 118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCCCGAA
 TTCTCGTGGA GACCCCGGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT
 138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCCGGCT
 GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTCGC CGCACGTGTG GAAGGGCCGA
 158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC
 CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCTGTCG
 178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A

SUBSTITUTE SHEET (RULE 26)

66EFG-4409660

661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC
AACCCGTGGG TCTGGATGTA GACGTGACAC TTAGTGTTCG GGTGTTGTG GTTCCACCTG
198 L G T Q T Y I C N V N H K P S N T K V D
721 AAGAAAGTTG AGCCCAATC TTGTGACAAA ACTCACACAT GA
TTCCTTCAAC TCGGGTTTAG AACACTGTTT TGAGTGTGTA CT
218 K K V E P K S C D K T H T O

FIG. 28B

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Variable Light Chain Domain

	10	20	abcde	30	40
6G425	DIVMTQTPLSLPVS LGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY				
	#	#	#	#	#
F(ab)-1	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY				
	#	#####			#
humkI	DIQMTQSPSSLSASVGDRVTITCRASKTI-----SKYLAWYQQKPGKAPKLLIY				
	=====				
	+++++				
	L1				

	50	60	70	80	90	100
6G425	YKVSNRFSGV PDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR					
	#	#	#	#####	#	#
F(ab)-1	YKVSNRFSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR					
	#	#	#	#	#####	#
humkI	YSGSTLES GVP SRFSGSGSGTDFTLTISLQPEDFATYYCQHNEYPLTFGQGTKVEIKR					
	===			=====		
	+++++			+++++		
	L2			L3		

Variable Heavy Chain Domain

	10	20	30	40
6G425	EIQLQQSGPELMKPGASVKISCKASGYFSSHYMHVWKQSHGKSLEWI			
	#	#	#	#
F(ab)-1	EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMHVWRQAPGKGLEWV			
	#	#	#	#
humIII	EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNWRQAPGKGLEWV			
	=====			
	+++++			
	H1			

	50	a	70	80	abc	90	100	110
6G425	GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT							
	#	#	#	#	#####	#	#	#
F(ab)-1	GYIDPSNGETTYNQKFKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT							
	#	#	#	#	#####	#	#	#
humIII	GMIHPSDSETRYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAARGIIFY-GTTYFDYWGQGT							
	=====				=====			
	+++++				+++++			
	H2				H3			

FIG. 29

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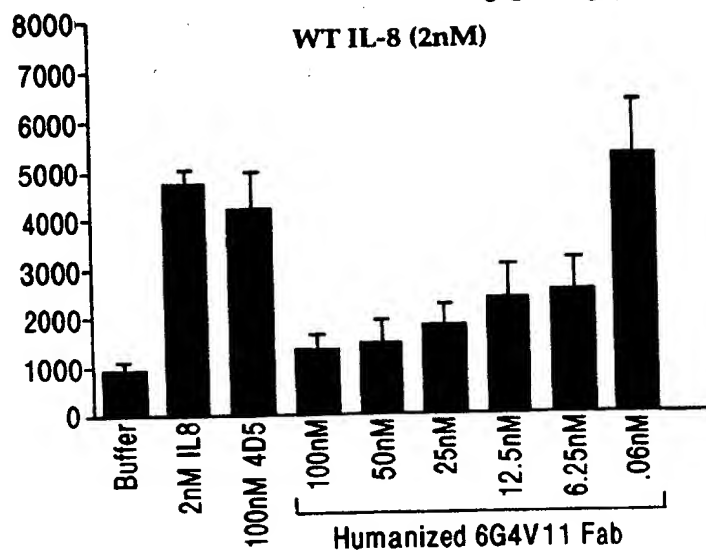


FIG. 30A

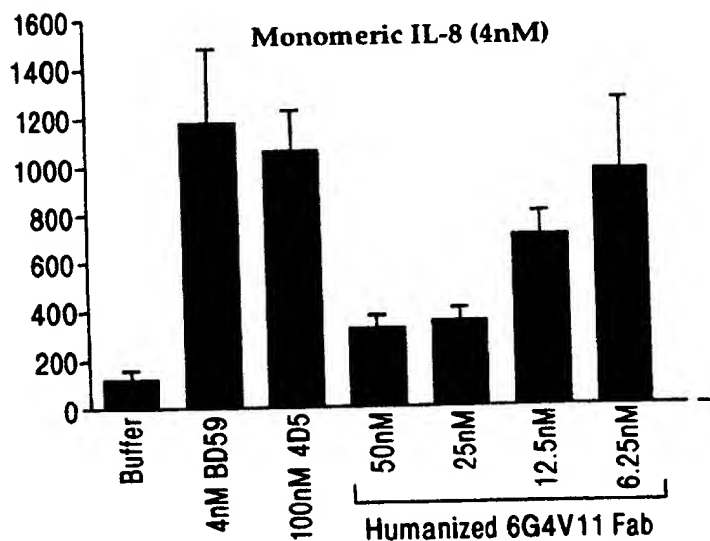
IC₅₀~12nM

FIG. 30B

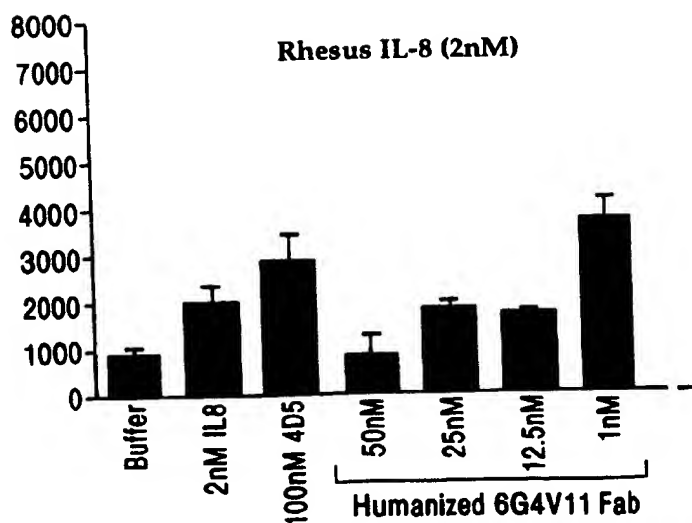
IC₅₀~15nM

FIG. 30C

IC₅₀~22nM

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPKGAPKLLIYKVSNRFSGVPSRFSGSGTDFTLTISSLQPEDFATYYCSQST
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVGYIDPSNGETTYNQKFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRNGDWFFDVGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVFSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT

Amino Acid Sequence of the peptide linker and M13 Phage Coat (gene-III)

SGGGSGGDFDYKMANANKGAMTENADENALQSDAKGLDSVATDYGAIDFIGDVS
GLANGNATGDFAGSSNSQMAQVGDGDN SPLMNNFRQYLPQLPQSV ECRPFVFSAGKPY
EFSIDCDKINLFRGVFAFLLYVATFMYVFSTFANILRNKES

FIG. 31A

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1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTCTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
18 R V T I T C R S S Q S L V H G I G N T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S Q S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCATTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCGTGG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C O

FIG. 31B

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGGTDFTLTISSLQPEDFATYYCSQST
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKDSITYSLSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVKQA
PGKGLEWVG
YIDPSNGET
TYNQKFKGR
FTLSRDNSK
NTAYLQMN
SLRAEDTAV
YYCARGDY
RYNGDWFF
DVWGQGT
LVTVSSAS
TKGPSVF
PLAPSSK
STSGGTA
ALGCLVK
DYFPEP
VTVSWNS
GALTSGV
HTFPAVL
QSSGLY
SLSSV
TVPSSSL
GTQTYI
CINVNH
KPSNTK
VDKKVEPKSCDKTHT

FIG. 31C



FIG.32

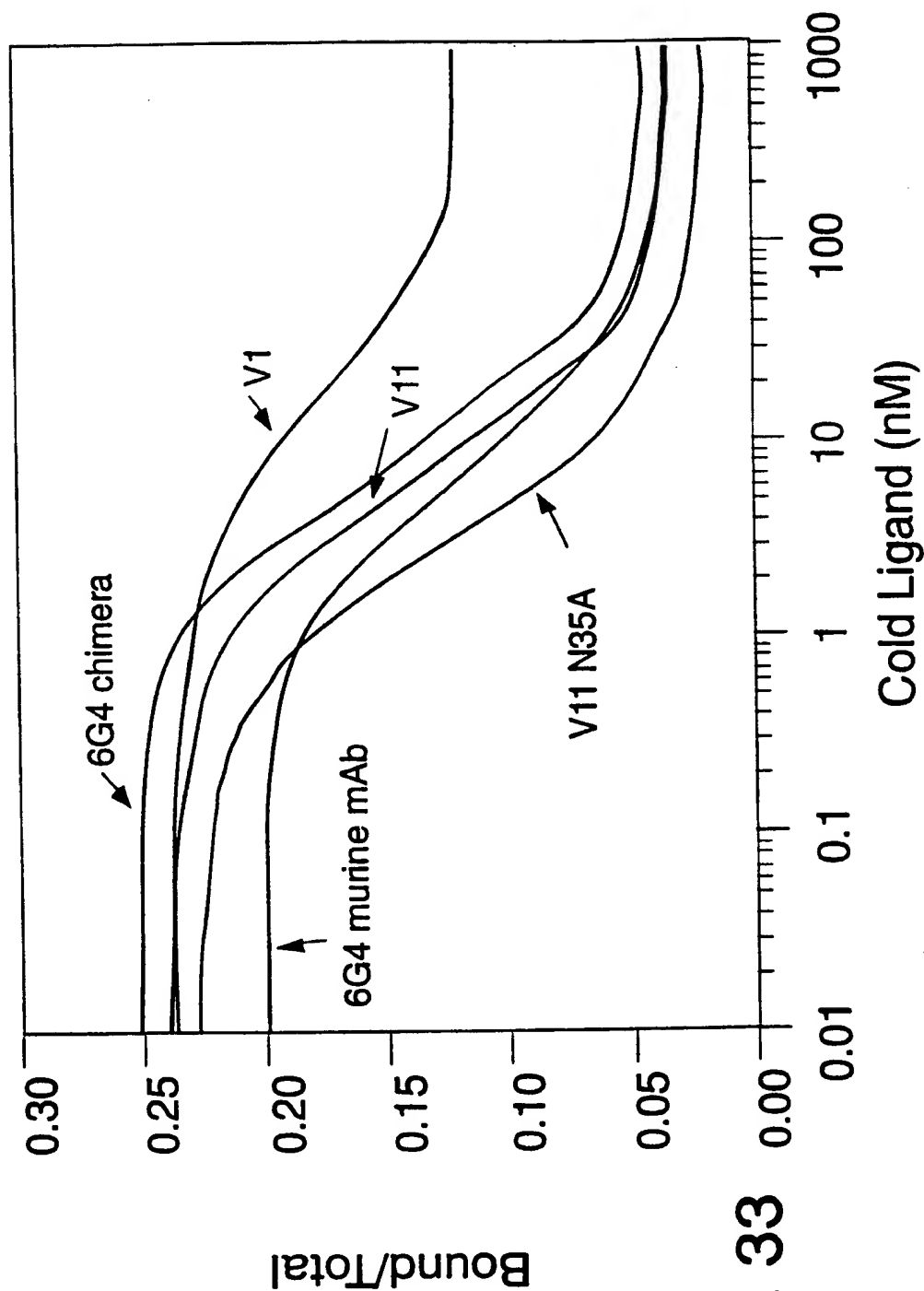
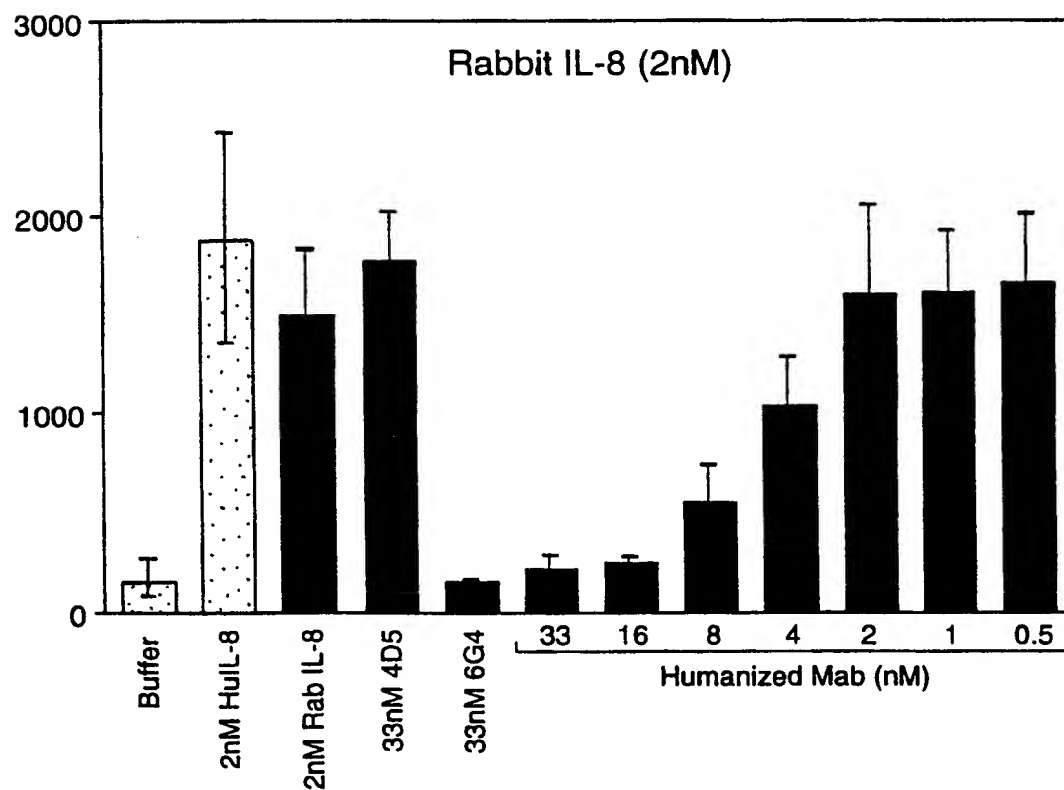
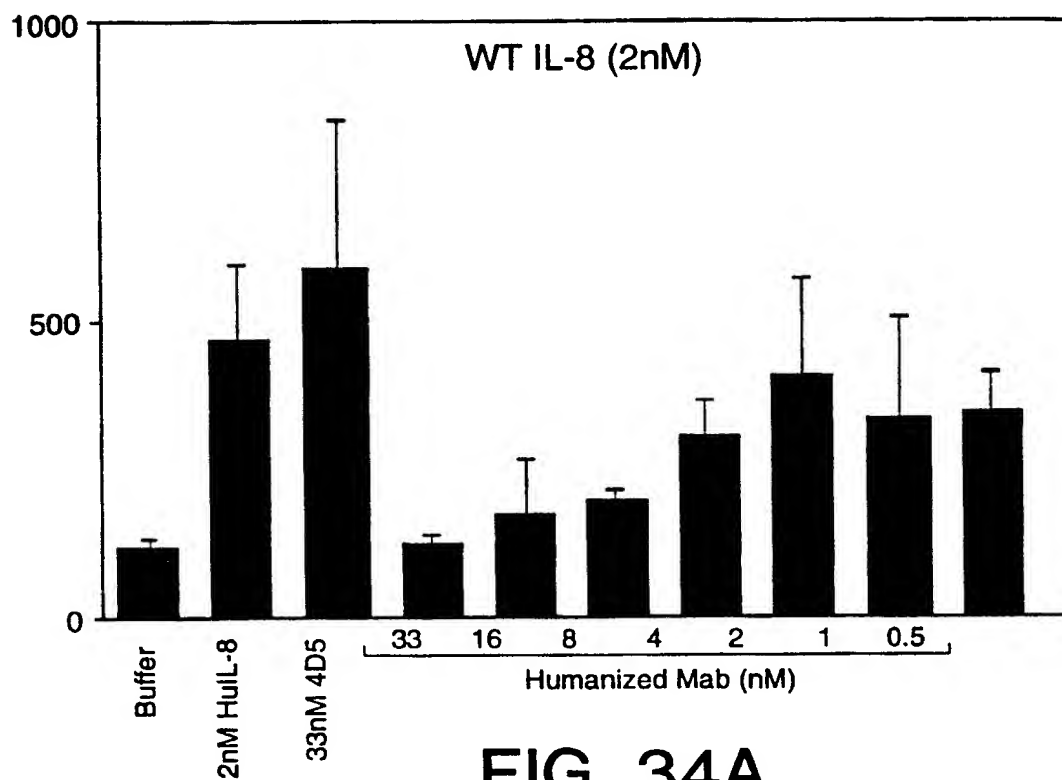


FIG. 33

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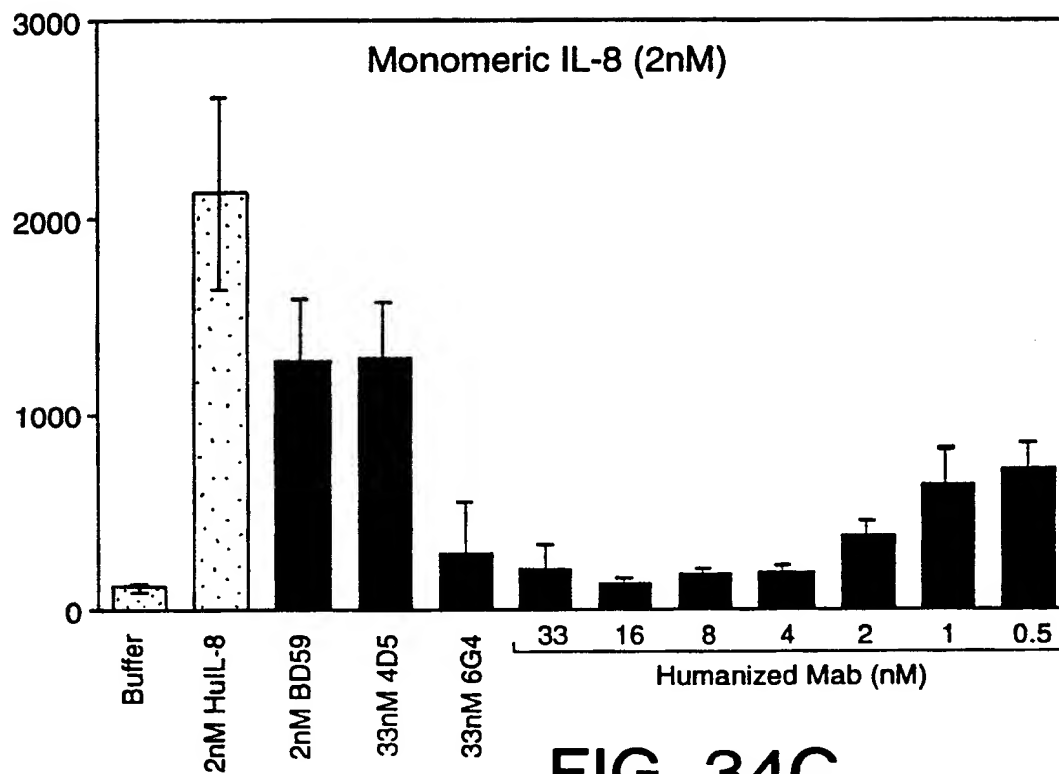


FIG. 34C

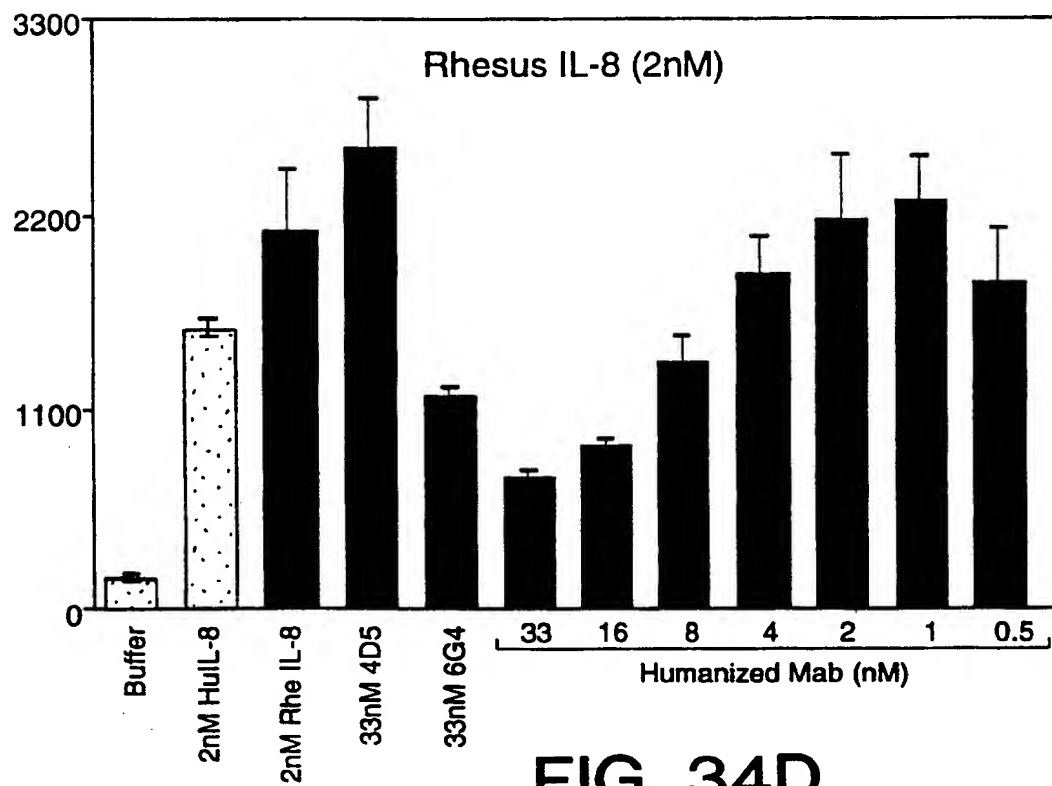


FIG. 34D

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Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain

MKKNIAFLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGATY
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGGSGDTFTLTISLQPEDEATYYCSQST
HVPLTFGQGTEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQWKVDN
ALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC

Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain

MKKNIAFLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH
WVRQAPGKGLEWVGVIDPSNGETTYNQFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY
CARGDYRYNGDWFFDVWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTK
VDKKVEPKSCDKTHT

Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper

CPPCPAPELLGGRMKQLEDKVEELL SKNYHLENEVARLKKLVGER

FIG. 35

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1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC
 TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
 -23 M K K N I A F L L A S M F V F S I A T N
 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
 -3 A Y A D I Q M T Q S P S S L S A S V G D
 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT
 TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA
 18 R V T I T C R S S O S L V H G I G A T Y
 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
 AATGTGACCA TAGTTGTCCT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
 38 L H W Y Q Q K P G K A P K L L I Y K V S
 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
 58 N R F S G V P S R F S G S G S G T D F T
 301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
 GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
 78 L T I S S L Q P E D F A T Y Y C S Q S T
 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
 GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
 98 H V P L T F G Q G T K V E I K R T V A A
 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
 118 P S V F I F P P S D E Q L K S G T A S V
 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
 138 V C L L N N F Y P R E A K V Q W K V D N
 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
 CGGGAGGTTA GCCCATTTGAG GGTCTCTCTCA CAGTGTCTCG TCCTGTCTGT CCTGTCTGTG
 158 A L Q S G N S Q E S V T E Q D S K D S T
 601 TACAGCCTCA GCAGCACCCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
 178 Y S L S S T L T L S K A D Y E K H K V Y
 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTCTCTGAA GTTGTCCCTT
 198 A C E V T H Q G L S S P V T K S F N R G
 721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
 CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGACCCGG GATCATGCGT TGATCAGCAT
 218 E C O

FIG. 36

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781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
TTTTCCCATG GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT
-1 M K K N I A F L L A

841 TCTATGTTCTG TTTTCTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
-11 S M F V F S I A T N A Y A E V Q L V Q S

901 GCGGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
8 G G G L V Q P G G S L R L S C A A S G Y

961 TCCTTCTCGA GTCACATAT GCACTGGGTC CGTCAGGCC CCGGTAAGGG CCTGGAATGG
AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTTCC GGACCTTACC
28 S F S S H Y M H W V R Q A P G K G L E W

1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAGTT CAAGGGCCGT
CAACCTATAT AACTAGGAAG GTTACCACCT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
48 V G Y I D P S N G E T T Y N O K F K G R

1081 TTCACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
AAGTGAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
68 F T L S R D N S K N T A Y L Q M N S L R

1141 GCTGAGGACA CTGCCGTCTA TTA CTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCTAA TAGCGATGTT ACCACTGACC
88 A E D T A V Y Y C A R G D Y R Y N G D W

1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
108 F F D V W G Q G T L V T V S S A S T K G

1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
128 P S V F P L A P S S K S T S G G T A A L

1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
CCGACGGACC AGTTCTCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
148 G C L V K D Y F P E P V T V S W N S G A

1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC
GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
168 L T S G V H T F P A V L Q S S G L Y S L

1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
TCGTGCGACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
188 S S V V T V P S S S L G T Q T Y I C N V

1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
TTAGTGTTCTG GGTCTGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
208 N H K P S N T K V D K K V E P K S C D K

1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA
TGAGTGTTGA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTGCGT
228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A

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1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTC TTGATGGTGG ATCTCTTACT TCACCGTTCT
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA
GAGTTTTTTCG AACAGCCCCT CGCGATT
268 L K K L V G E R O

FIG. 37B

477,136

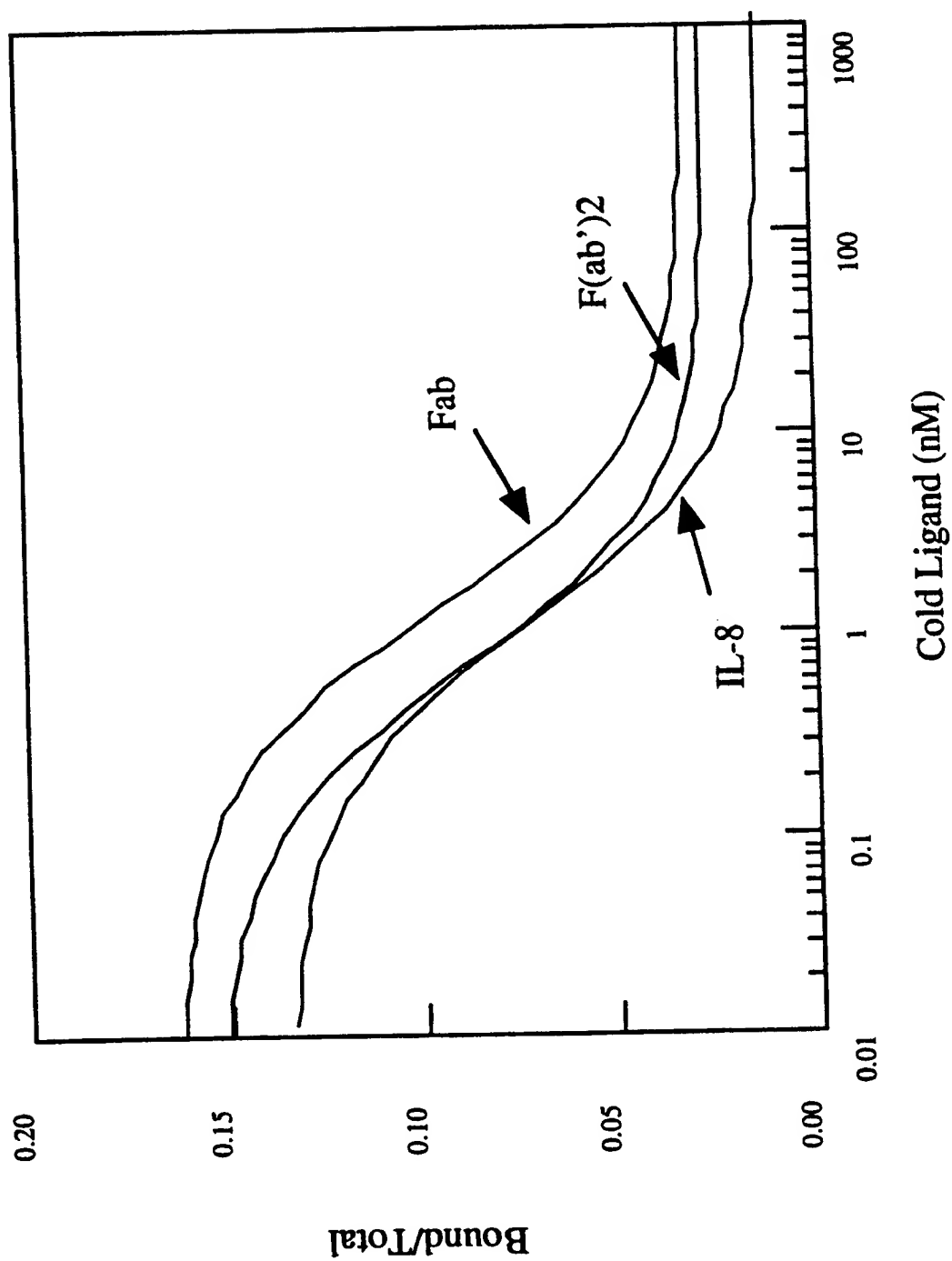


FIG. 38

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FIG. 39

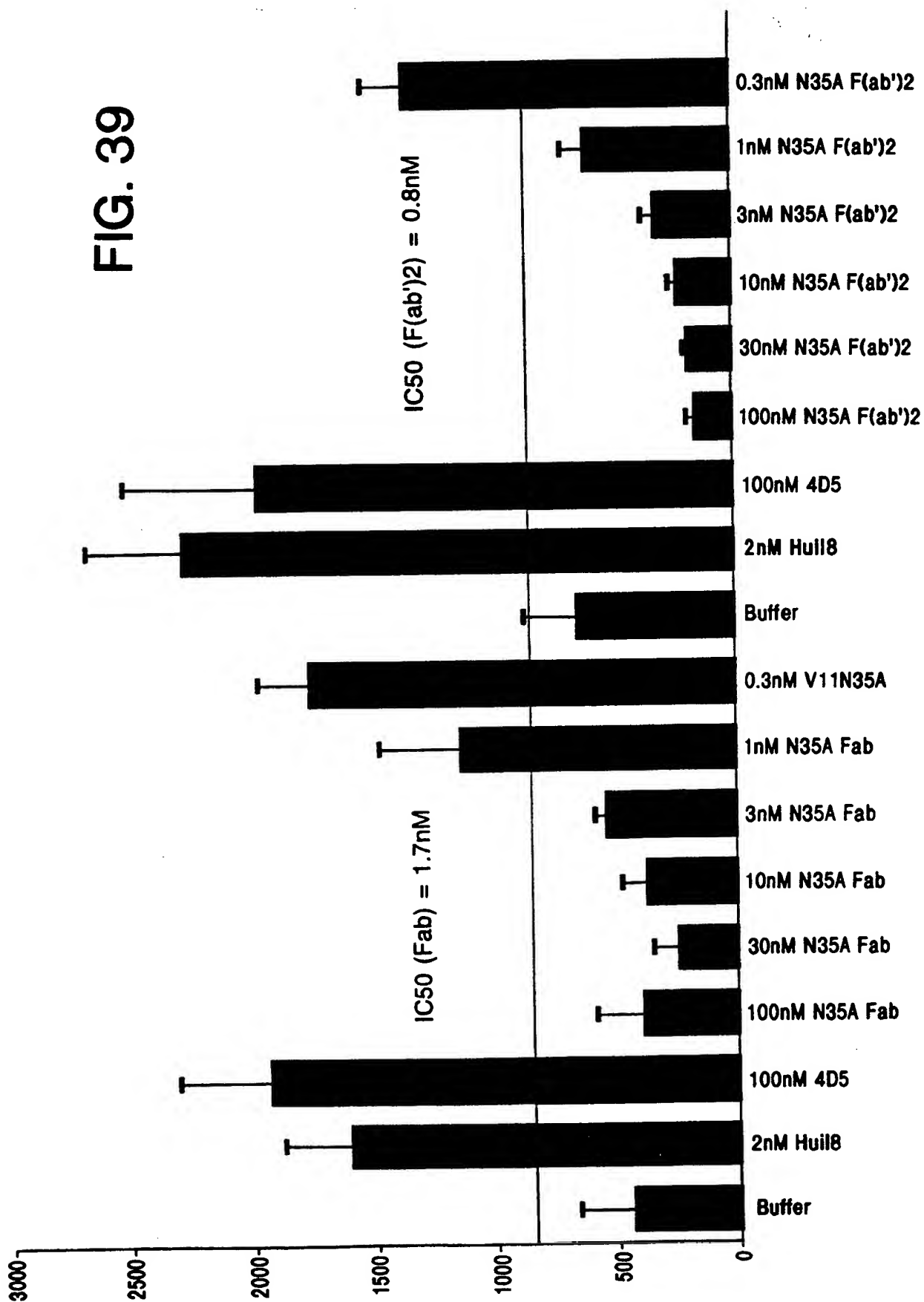


FIG. 40

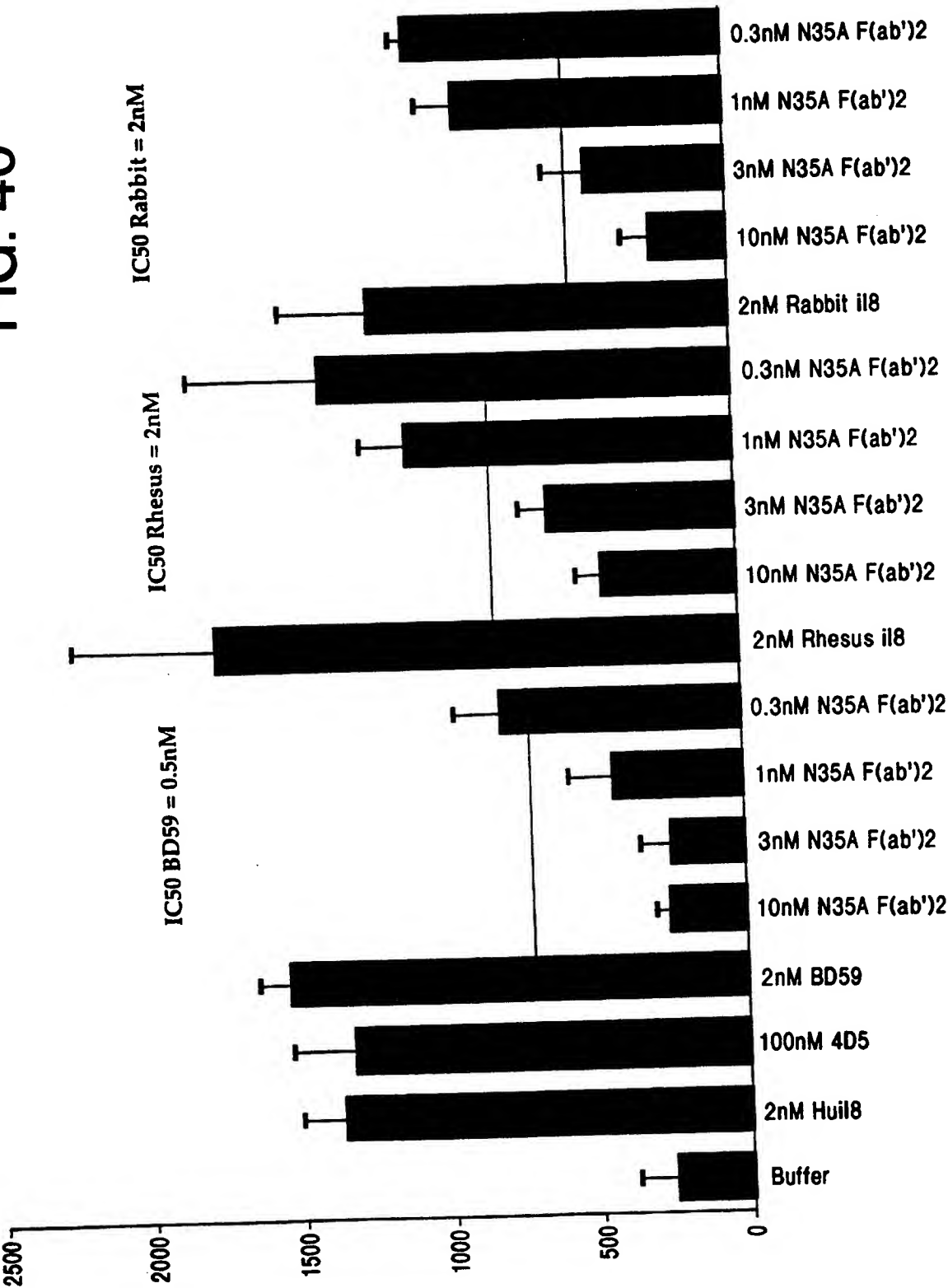


FIG. 41A

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scrFI
 nciI
 mspI
 hpaII
 dsav
 xmaI/pspAI
 smaI
 scrFI
 nciI
 dsav
 cauII
 bsaJI
 avai
 rsaI
 csp6I
 nlaIV
 kpnI
 hgiCI
 bani
 asp718
 acc65I
 401 TCGGTACCCG GGGATCCTCT CGAGGTGAG GTGATTTAT GAAAAGAAAT ATCGCATTC TTCTTGCATC TATGTCGTT TTTTCTATTG CTACAACGC
 AGCCATGGC CCTAGGAGA GTCCAACTC CACTAAATA CTTTTCTTA TAGCGTAAAG AAGAACGTAG ATACAAGCAA AAAAGATAAC GATGTTGCG
 M K K N I A F L L A S M F V F S I A T N A
 a mutation was found that inactivated the mluI site. The penultimate nucleotide was changed fr G toT ^

mboII
 sfaNI
 hphI
 mnlI
 bsmFI
 bmyI
 bsrI
 tth111I/aspI
 ecorV
 501 ATACGCTGAT ATCCAGATGA CCCAGTCCC GAGTCCCCTG TCCGCCTCTG TGGCGCATAG GGTACCATC ACCTGCAGGT CAAGTCAAG CTAGTACAT
 TATCGGACTA TAGGTCTACT GGGTCAGGG CTGAGGGGAC AGCGGGAGAC ACCCGCTATC CCAGTGGTAG TGGACGTCCA GTTCAGTTTC GAATCATGTA
 -2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

sstI
 sacI
 hgiJII
 hgiAI/aspHI
 ecl136II
 bsp1286
 bsiHKAI
 bsmFI
 bmyI
 bsrI
 tth111I/aspI
 ecorV
 501 ATACGCTGAT ATCCAGATGA CCCAGTCCC GAGTCCCCTG TCCGCCTCTG TGGCGCATAG GGTACCATC ACCTGCAGGT CAAGTCAAG CTAGTACAT
 TATCGGACTA TAGGTCTACT GGGTCAGGG CTGAGGGGAC AGCGGGAGAC ACCCGCTATC CCAGTGGTAG TGGACGTCCA GTTCAGTTTC GAATCATGTA
 -2 Y A D I Q M T Q S P S S L S A S V G D R V T I T C R S S Q S L V H

bspMI
 scfI
 pstI
 sse8387I
 hphI
 maeII
 bstEII
 hphI
 bsgI
 ddeI
 nlaIII
 aluI
 rsaI
 hindIII
 csp6I
 CAAGTCAAG CTAGTACAT
 GTTCAGTTTC GAATCATGTA

FIG. 41B

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```

        scrFI      tfil      hinfi      bsmFI
        mval      taqi      bsmI/gsuI[dcM-]
        ecorII     clai/bsp106      pleI
        dsav      bspDI[dam-]      hinfi
        bstNI      aluI
        apyI[dcM+]
601 GGTATAGGTG CTACGTATTT ACACGTGGTAT CAACAGAAAC CAGGAAAGC TCCGAACTA CTGATTACA AAGTATCCAA TCGATTCTCT GGAGTCCCTT
    CCATATCCAC GATGCATAA TGTGACCATA GTTGCTTTTG GTCCCTTTTG AGGCTTGAT GACTAATGT TTCATAGGT AGCTAAGAGA CCTCAGGGAA
32 G I G A T Y L H W Y Q Q K P G K A P K L L I Y K V S N R F S G V P S

        mspI
        hpaII
        bslI
        bsaWI
        sau3AI
        mboI/ndeII[dam-]
        dpnI[dam+]
        dpnII[dam-]
        alwI[dam-]
        nlaIV
        bstVI/xhoII
        bamHI
        alwI[dam-]      bsmFI
66  CTCGTTCTC TGTATCCGGT TCTGGGACGG ATTTCACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTCAC AGAGTACTCA
    GAGCGAAGAG ACCTAGGCCA AGACCCTGCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA CGGTGAATA ATGACAAGTG TCTCATGAGT
        R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C S Q S T H
        styI
        bsaJI
        isaI
        csp6I
        nlaIV
        kpnI
        hgiCI
        bani
        asp718
        acc65I
        maeII
        bsmFI
        bsrBI
        acII
        bsmFI
801 TGTCCTGCTC ACGTTTGGAC AGGTATCCAA GGTGGAGATC AAACGAACTG TGGCTGCACC ATCTGCTTC ATCTTCCCGC CATCTGATGA GCAGTTGAAA
    ACAGGGCGAG TGCAACCTG TCCCATGGTT CCACCTCTAG TTTGCTTGAC ACCGACGTCG TAGACAGAAG TAGAAGGGCG GTAGACTACT CGTCAACTTT
        mboII
        bpuAI
        bbsI
        mboII
        aciI
99 V P L T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K

```

FIG. 41C

FIG. 41D

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rmaI
 maeI
 bfaI
 xbaI mnlI mnlI
 hphI
 mboII sfaNI
 1201 AGTACGCAAC TAGTCGTAA AAGGGTATCT AGAGGTTGAG GTGATTTTAT GAAAAGAAAT ATCGCATTC TTCTGCATC TATGTCGTT TTTCTATTG
 TCATGCGTTG ATCAGCATTT TTCCCATAGA TCTCCAATC CACTAAATA CTTTTCTTA TAGCGTAAAG AAGAAGCTAG ATACAGCAAA AAAAGATAAC
 M K K N I A F L L A S M F V F S I A

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scrFI
 mvaI
 ecorII
 dsav
 scrFI
 mvaI fnu4HI
 ecorII
 dsav bstNI hgiII
 bstNI bsoFI bsp1286
 apyI[dcM+] bsaJI bmyI
 haeIII/palI apyI[dcM+]
 acilI haeI bbvI banII
 1301 CTACAAACG GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCTG GTGCAGCCAG GGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC
 GATGTTTGG CATGCGACTC CAAGTCGATC ACGTCAGACC GCCACCGGAC CACGTGCTC CCCCAGCTGA GGCAACAGG ACACGTCGAA GACCGATGAG
 -5 T N A Y A E V Q L V Q S G G G L V Q P G G S L R L S C A A S G Y S

scrFI
 nciI
 mspI
 hpall
 dsav
 caulI
 bsli
 xmaI/pspAI
 smaI
 scrFI
 nciI
 dsav
 caulI
 bsli

scrFI
 mvaI
 ecorII

FIG. 41E

pleI
 hinfi
 taqi
 xhoI
 pae7I
 aval
 maeIII
 CTTCTCGAGT CACTATATGC ACTGGGTCCG
 1401 GAAGAGCTCA GTGATATACG TGACCCAGGC AGTCCGGGCG CCATTCCCGG ACCTACCCCA
 29 F S S H Y M H W V R Q A P G K G L E W V G Y I D P S N G E T T Y N
 dsav
 bstNI
 bsaiI
 sau96I
 nlaIV
 haeIII/pali
 asuI
 eco0109I/draII
 haeIII/pali
 eco0109I/draII
 TCGAATGGGT TCGATATATT GATCCTTCCA ATGCTGAAC TACGTATAAT
 1501 CAAAAGTTCA AGGCCCGTTT CACTTTATCT CGCACAAC AGCATACTG CAGATGAACA GCCTGGCTGC TGAGGACACT GCCGCTCAT
 GTTTTCAAGT TCCCGGCAAA GTGAATAGA GCGTGTGA GGTTTTGTG TCGTATGAC GTCTACTGT CGGACGACG ACTCCTGTGA CGGCAGATAA
 62 Q K F K G R F T L S R D N S K N T A Y L Q M N S L R A E D T A V Y Y
 haeIII/pali
 sau96I
 asuI
 nruI
 haeIII/pali
 bstUI
 bsh1236I
 thal
 fnuDII/mvni
 scfI
 pstI
 bsgI
 bspMI
 cac8I
 ddeI
 drdI
 sau96I
 nlaIV
 hgiJII
 bsp1286
 bsp120I
 maeIII
 bstEII
 scrFI
 mvaI
 ecorII
 dsav
 bstNI
 bsaJI
 hphI
 bsmBI
 nlaIV
 apyI[dcm+] bsmAI
 nlaI
 bseRI
 esp3I
 bsaJI
 hphI
 bsmBI
 nlaIV
 apyI[dcm+] bsmAI
 haeIII/pali
 eco0109I/draII
 TCGGCTTCCA CCAAGGGCCC
 1601 ACTGTGCAAG AGGGGATTAT CGCTACAATG GTGACTGGTT CTTCGACGTC TGGGTCAAG GAACCTTGGT CACGCTCTCC TCGGCTTCCA CCAAGGGCCC
 TGACACGTTT TCCCCTAATA GCGATGTTAC CACTGACCAA GAAGCTGCAG ACCCAGTTC CTTGGGACCA GTGGCAGAGG AGCCGAGGT GGTTCGCGG
 96 C A R G D Y R Y N G D W F F D V W G Q G T L V T V S A S T K G P
 seq right is from p6G425chim2.fab2

FIG. 41F

FIG. 41G

[illegible]

FIG. 41H

2501 AATGCGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG CTGTAGGCAT AGGCTTGCTT ATGCCGGTAC TGCCGGGCTT CTTCGGGGAT ATCGTCCATT
TTACGGGAGT AGCAGTAGGA GCCGTGGCAG TGGACCTTAC GACATCCGTA TCCGAACCAA TAGCGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA

2401 CCACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT ATATGCGTTG ATGCAATTC TATGGCACC CGTTCTCGGA GCACGTGTCG ACCGCTTGG
GGCTGTCGTA GCGGTCAAGT ATACCGCAG ACATCGCGA TATACGCAAC TACGTTAAG ATACGGCTGG GCAAGAGCCT CGTGACAGGC TGGCGAACC

2501 CCGCGCGGCT CAGGACGAGC GAAGCGATGA ACCTCGGTGA TAGCTGATGC GCTATACCG CTGCTGTGG CAGGACACCT AGGAGATGCG GCCTGCGTAG

FIG. 41I

FIG. 41J

acII
 thal
 fnuDII/mvnl
 bstUI nlaIII
 bsh1236I
 hinPI bcgI
 hhai/cfoI
 acII
 fnu4HI
 bsoFI
 mboII
 bpuAI
 bbsI
 nlaIII
 banI hpaII hhai/cfoI
 hgiCI bbvI
 nlaIV bsoFI
 cac8I eco47III
 cfr10I/bsrFI
 nael haeII
 mspI hinPI
 fnu4HI
 2901 TGGGCGGG GCATGACAT CGTCGCCGCA CTTATGACTG TCTTCTTTAT CATGCAACTC GTAGGACAGG TGCCGGCAGC GCTCTGGTC ATTTTCGGCG
 ACCGCGCCC CGTACTGATA GCAGCGCGCT GAATACTGAC AGAAGAAATA GTACGTTGAG CATCCTGTCC ACGGCCGTG CGAGACCCAG TAAAGCCGC
 thal
 fnuDII/mvnl
 bstUI haeIII/palI
 bsh1236I sau3AI
 hinPI mboI/ndeII[dam-]
 hhai/cfoI dpuI[dam+]
 bpmI/gsuI[dcM-] dpuII[dam-]
 acII
 sau96I
 avaII
 asuI
 3001 AGGACCGCTT TCGCTGGAGC GCGACGATGA TCGGCCTGTC GCTTGGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGCC TTGCTCACTG GTCCCCGCC
 TCCTGGCGAA AGCGACCTCG CGCTGCTACT AGCCGGACAG CGAACGCCAT AAGCCTTAGA ACGTGCGGA GCGAGTTCGG AAGCAGTGAC CAGGCGGTG
 mcrI
 eagI/xmaII/ecI XI
 eaeI hinPI
 cfrI hhai/cfoI
 bsiEI thal
 mspI
 nael
 cfr10I/bsrFI
 fnu4HI
 fnuDII/mvnl
 bstUI
 bsh1236I
 haeIII/palI hpaII
 bsoFI
 acII hgaI
 cac8I
 bgII nlaIII haeIII/palI
 maeII
 cac8I
 nruI bsh1236I foki haeIII/palI
 thal
 hgaI
 thal fnuDII/mvnl
 fnuDII/mvnl
 bstUI bstUI
 bsh1236I mnlI
 haeI
 maeII
 psp1406I
 3101 CAAACGTTTC GCGGAGAAGC AGGCCATTAT CGCGGCATG GCGGCCGACG CGCTGGGCTA CGCTTGCTG CGCTTCGCA GCGAGGCTG GATGGCCTTC
 GTTTCGAAAG CGCTCTTCG TCCGGTAATA GCGCGCTGAC CGCGGCTGC GCGACCCGAT GCAGAACGAC CGCAAGCGCT GCGCTCCGAC CTACCGGAAG

FIG. 41K

SUBSTITUTE SHEET (RULE 26)

fnu4HI
 bsoFI
 aciI
 thaI
 fnuDII/mvni
 bstUI
 cac8I
 sau3AI bsh1236I
 mboI/ndeII[dam-]
 dpnII[dam+]
 dpnII[dam-]
 taqI[dam-]
 sau3AI asuI
 mboI/ndeII[dam-]
 dpnI[dam+] nspBII
 dpnII[dam-]
 bsrI
 sau3AI
 mboI/ndeII[dam-]
 sau96I
 avaII
 mnII
 bsaJI
 aciI
 fnu4HI
 bsoFI
 bgII
 cac8I
 nlaIII
 nlaIII
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 bmyI
 cac8I
 nlaIII
 CTAGCGAGCG CCGAGAAATGG TCGGATTGAA GCTAGTGACC TGGCGACTAG CAGTGCCGCT AGCCTAACIT CGATCACTGG ACCGCTGATC GTCACGGCGA TTTATGCCGC CTCGGCGAGC ACATGGAACG GGTGGCATG GATCGCTCG GGCCTTTACC AGCCTAACIT
 3301

[illegible]

FIG. 41L

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hphI pflMI bsmI nlaIV nlaII acil hgaI
 tfil hinfI bsh1236I thal acil
 fnuDII/mvni bstUI bsh1236I
 3501 CTAACGGATT CACCACTCCA AGAATTGGAG CCAATCAATT CTTCGGGAGA ACTGTGAATG CGCAAAACCAA CCCTTGGCAG AACATATCCA TCAGGTCCGC
 GATTGCCCTAA GTGGTGAGGT TCTTAACCTC GGTTAGTTAA GAACGCTCTT TGACACTTAC CGGTTTGGTT GGAACCCGTC TTGTATAGGT AGCCAGGCG

hinPI hhaI/cfoI mstI pflMI styI
 avIII/fspI bsmI bslI bsaJI
 haeIII/palI mscI/balI haeI
 scrFI mvaI dsal ecorII dsav bstNI
 bslI bsaJI apyI[dcM+] sau96I
 fnu4HI thal hinPI fnu4HI bsoFI fnuDII/mvni
 bsoFI bstUI fnu4HI hhaI/cfoI hhaI/cfoI fnu4HI
 bsoFI cac8I bsh1236I avarI bsoFI
 bbVI acil bsh1236I acil sfanI
 bpmI/gsuI[dcM-] acil sfanI
 3601 CATCTCCAGC AGCCGCACGC GCGCATCTC GGCAGCGGT GGCCTCGGAG CCCGTCGCAA CCCAGGACCG GTGCCACGC GTACTAGCAC GAGGACAGCA ACTCCTGGGC CGATCCGACC

mspI hpaII scrFI nciI dsav sau96I
 nlaIV avarI asuI rmaI maeI
 ecoO109I/draII mnlI cauII-bfaI acil
 fnu4HI bsoFI bbVI fnu4HI bsoFI bbVI maeI ddel nlaIII
 cac8I thal fnuDII/mvni bstUI bsh1236I maeI
 bsh1236I maeI
 bsrI bsh1236I maeI
 3701 CGGGGTGCC TTACTGGTTA GCAGAATGAA TCACCGATAC GCGAGCGAAC GTGAAGCGAC TGCTGTGCA AACGTCTGC GACCTGAGCA ACAACATGAA
 GCCCCAACGG AATGACCAAT CGTCTTACTT AGTGGCTATG CGCTCGCTTG CACTTCGCTG ACGACGACGT TTTCGACAGC CTGGACTCGT TGTGTACTT

FIG. 41M

sau3AI
mboI/ndeII[dam-]
mami[dam-]
dpmI[dam+]
dpmII[dam-]
bstYI/xhoII
alwI[dam-]
mspi
hpaII
mroI bsaBI[dam-]
bspMI
bspEI[dam-]
bsaWI sfaNI
accIII[dam-]
fnu4HI
bsoFI
bbvI
sfaNI
fokI cac8I
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
AATACAAGGC CTAGACGTAG CGTCCTACGA CGACCGATGG

3801 TGGTCTTCGG TTTCCGGTGT TCGTAAAGTC TGGAAACGGC GAAGTCAGCG CCCTGCACCA TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
ACCAAGGCC AAAGGCACAA AGCATTTTCAG ACCTTTGCGC CTTCACTGCG GGGACGTGGT

acII
thai
fnuDII/mvni hinPI
bstUI hhaI/cfoI
bsh1236I haeII mslI
cac8I
hinPI
hhaI/cfoI
tru9I haeII
mseI eco47III
dcl
TGACCCCTGAG TGACCTGGCAT GCGCTGGCAA TATTAACGAA GCGCTGGCAT TGACCCCTGAG TGATTTTCT CTGGTCCGC CGCATCCATA CCGCCAGTTG TTTACCCCTCA
GACACCTTGT GGATGTAGAC ATAATTGCTT CCGCACCGTA ACTGGGACTC ACTAAAGA GACCAGGCG CCGTAGGTAT GGCGGTCAAC AAATGGGAGT

4001 CTAACGTTCCA GTAACGGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCCTCTCT CGTTTCATCG GTATCATTCAC CCCCATGAAC AGAAATTCCTC
GTTGCAAGGT CATTGGCCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGGG

FIG. 41N

FIG. 410

4401 CGGGTGTGG hgiAI/aspHI
 GCCCACAGCC bsp1286
 fnu4HI bsoFI bsiHKAI
 bsoFI bsvI bmyI ndeI
 hinPI nlaIII bsrI bsaAI maeII
 hhaI/cfoI tth111I/aspI maeIII
 bst1107I tru9I bsoFI
 acII accI bsrI mseI
 acII acII AACTATGCGG CATCAGAGCA GATTGTACTG AGAGTGCACC
 AGCGGAGTGT ATACTGGCTT AACTATGCGG CATCAGAGCA GATTGTACTG AGAGTGCACC
 TGACCCAGTC ACCTAGCGAT AGCGGAGTGT ATACTGGCTT AACTATGCGG CATCAGAGCA GATTGTACTG AGAGTGCACC
 ACTGGGTGCT ACTGGGTGCTA TGCATCGCTA TCGCCTCACA TATGACCGAA TTGATACGCC GTAGTCTCGT CTAACATGAC TCTCAGGTGG
 4501 ATATCGGGTG TGAATACCG CACAGATGCG TAAGGAGGAA ATACCGCATC AGCGCTCTT CCGCTTCCCTC GCTCACTGAC TCGCTGCGCT mcrI
 TATAGGCCAC ACTTATGGC GTGTCTACGC ATTCTCTTTT TATGGCGTAG TCCGCGAGAA GCCGAAGGAG CGAGTGACTG AGCGACGCGA GCCAGCAAGC bsiEI
 acII acII sfanI
 fnu4HI bsoFI
 acII acII
 fnu4HI bsoFI pleI bsoFI mcrI
 bsvI bsrBI aluI bsoFI bsvI bsiEI
 bsvI cac8I
 GCTGCGCGA GCGGTATCAG CTCACCTCAA GCGGGTAATA CCGTTATCCA CAGATCAGG GGATAACGCA GTGAGGCAAA AGGCCAGCAA
 CGACGCGCT CGCCATAGTC GAGTGAGTTT CGCCATTAT GCCAATAGGT GTCTTAGTCC CCTATTGCGT CCTTTCTTGT ACACCTCGTT TCCGGTCTGT
 4601 scrFI thaI fnuDII/mvnI
 mvaI bstOI
 ecoRII bsh1236I
 dsav bstNI bslI
 bstNI bslI
 apyI[dcM+] fnu4HI
 haeIII/palI bsoFI cac8I
 haeIII/palI bsoFI haeIII/palI
 haeI nlaIV
 4701 AAGGCCAGGA ACCGTAAAAA GGCCGCGTTG CTGGCGTTTT TCCATAGGCT CCGCCCCCCT GACGAGCATC ACAAATCG ACGTCAAGT CAGAGGTGGC
 TTCCGGTCTT TGGCATTTTT CGGGCGCAAC GACCGCAAAA AGGTATCCGA GGCGGGGGA CTGCTCGTAG TGTCTTTAGC TCGAGTTCA GTCTCCACCG
 hgaI
 drdi
 tagI
 sfanI
 mnlI

FIG. 41P

FIG. 41Q

FIG. 41R

[illegible]

FIG. 41S

FIG. 41T

(26) ע"פ דברי רש"י שם

FIG. 41U

```

>length: 6563

aatII(GACGTC):      1645 6489
acc65I(GGTACC):      403 823
acci(GTMKAC):      1093 1963 4449
accIII(TCCGGA):      3867[dam-]
aciI(CCGC):      178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
                3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
                4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
                5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
acyI      see hinII
aflIII(ACRYGT):      1307 4678
ageI(ACCGGT):      1788
ahaII/bsaHI(GRCGYC):      1645 1813 2616 2637 2751 3408 6107 6489
ahaIII/draI(TTTAAA):      5435 5454 6146
ahdI/eam1105I(GACNNNNNGTC):      346 5566
aluI(AGCT):      72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
                2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
                5922
alw44I/snoI(GTGCAC):      1831 4494 4992 6238
alwI[dam-](GGATC):      412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                6196 6214
alwNI[dcn-](CAGNNNCTG):      1117 1385 5089
apaI(GGGCCC):      1695
apaLI/snoI(GTGCAC):      1831 4494 4992 6238
apoI(RAATTY):      1 391 4093
apyI[dcn+](CCWGG):      640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asnI/vsPI(ATTAAAT):      5742
asnI      see aseI
asp700(GAANNNTTC):      905 930 4234 6166
asp718(GGTACC):      403 823
aspHI      see hgiAI
aspi      see tth111I
asuI(GGNCC):      1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463

```

FIG. 41V

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Stop Template Primer

SL.97.2 5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3'

NNS Randomization Primer

SL.97.3 5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3'

FIG. 42

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Randomization of Position N35 of Variable Light Chain CDR-1
Amino Acid Frequency

Phage Display (NNS Codon Library) Sort #3

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

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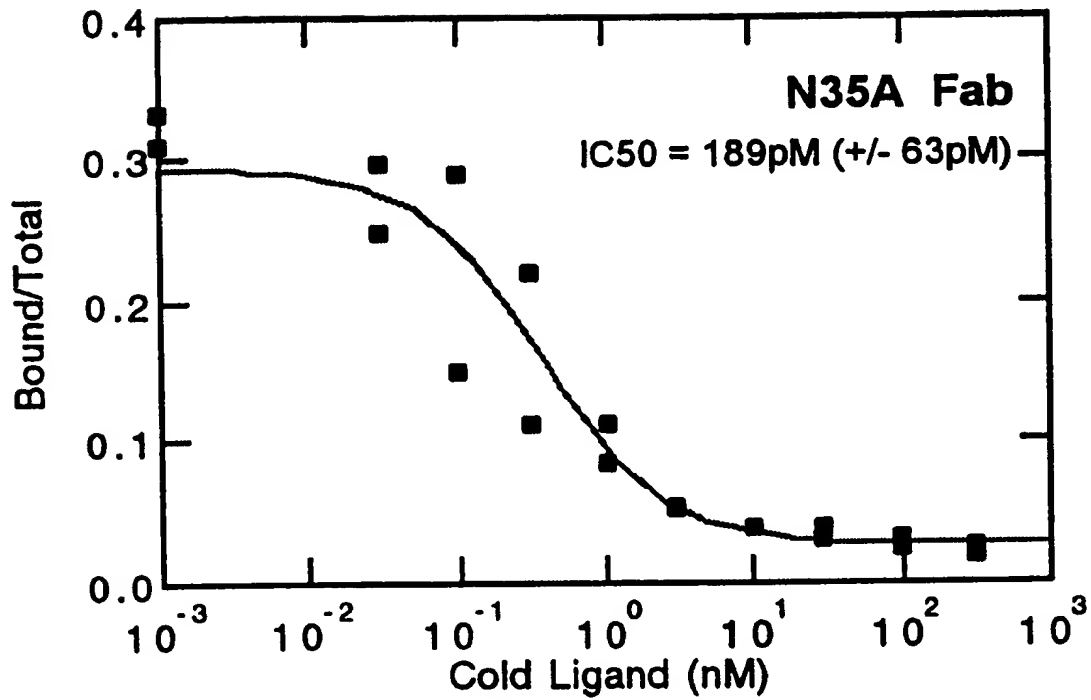


FIG. 43B-1

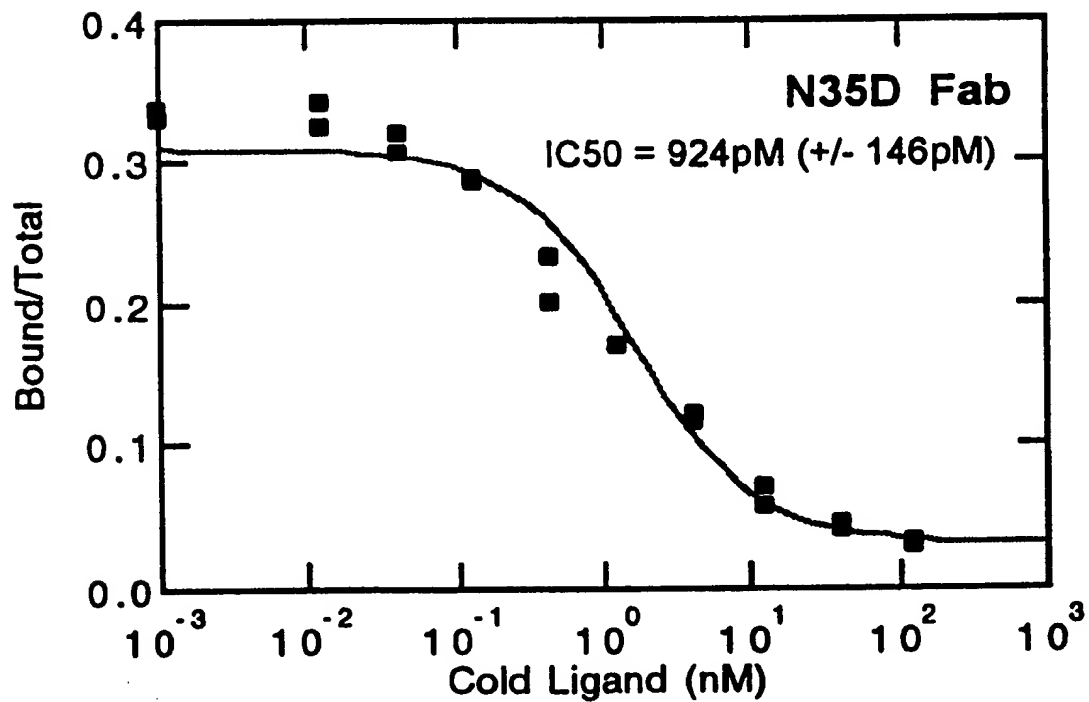


FIG. 43B-2

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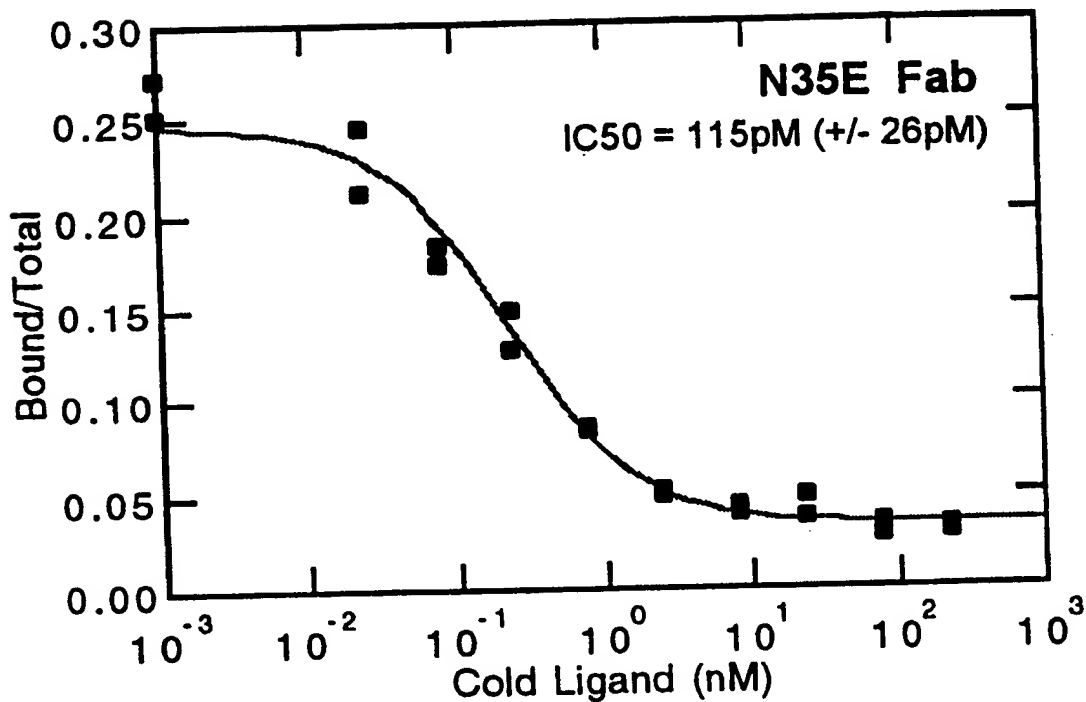


FIG. 43B-3

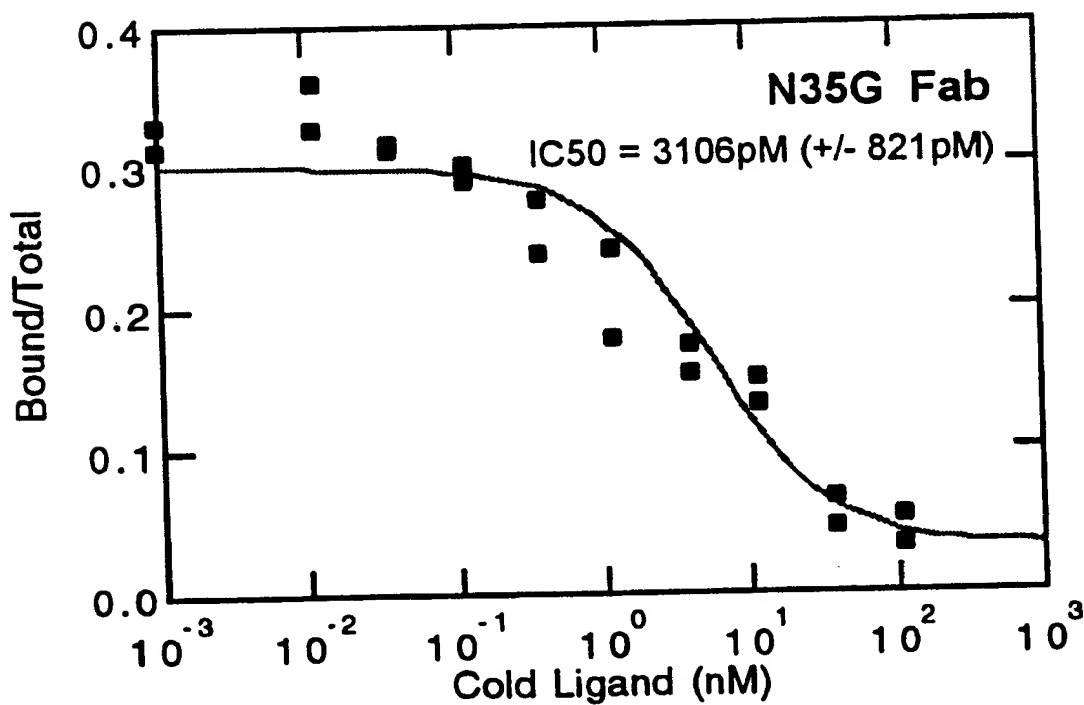
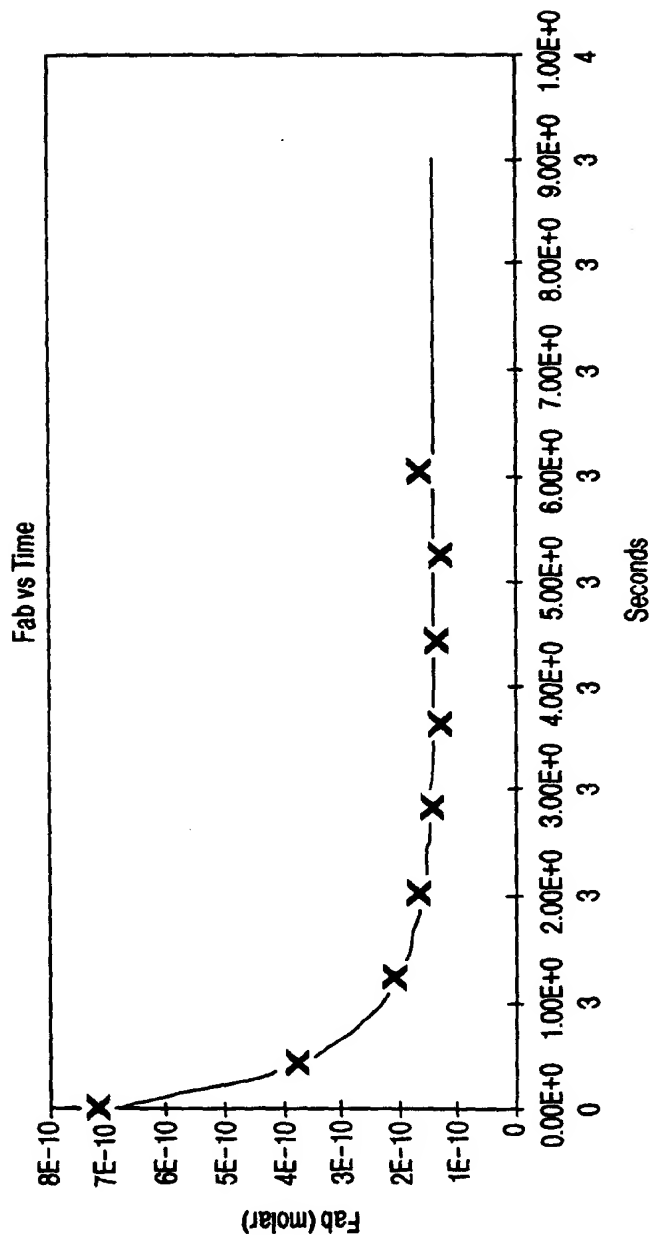


FIG. 43B-4

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Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')₂.

SAMPLE	ka	kd	Kd
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') ₂	2.0x10 ⁶	2.1x10 ⁻⁴	109pM
6G4V11N35E-Fab	4.7x10 ⁶	2.6x10 ⁻⁴	54pM

FIG. 44

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1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTTTCTAT TGCTACAAAC
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCGCGCTC TGTGGGCGAT
CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA
-3 A Y A D I Q M T Q S P S S L S A S V G D

121 AGGGTCACCA TCACCTGCAG GTC AAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT
TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA
18 R V T I T C R S S O S L V H G I G E T Y

181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC
AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG
38 L H W Y Q Q K P G K A P K L L I Y K V S

241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT
TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA
58 N R F S G V P S R F S G S G S G T D F T

301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT
GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA
78 L T I S S L Q P E D F A T Y Y C S O S T

361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA
GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT
98 H V P L T F G Q G T K V E I K R T V A A

421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT
GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA
118 P S V F I F P P S D E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC
CGGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTTG
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG
178 Y S L S S T L T L S K A D Y E K H K V Y

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA
CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCTT
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA
CTCACAATTG GACTAGGAGA TCGGCCTGCG GTAGCACCGG GATCATGCGT TGATCAGCAT
218 E C Q

FIG. 45

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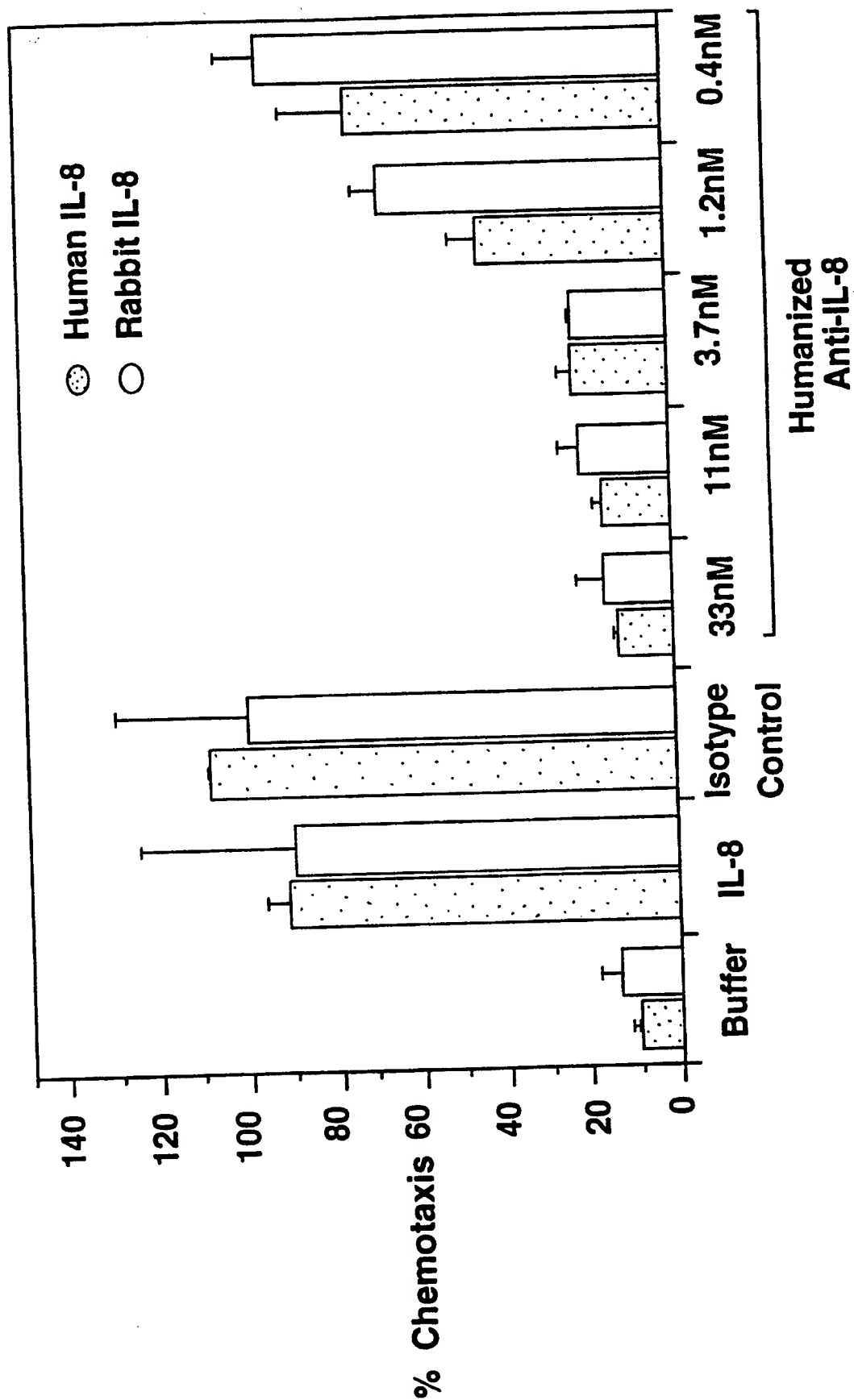


FIG. 46

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N35AH1upr
5'-CTAGTGCAGTCTGGCGGTGGCCTGGTGCAGCCAGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGGCTACTCCTTC-3'

N35AH1lwr
5'-TCGAGAAGGAGTAGCCAGAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAAGGCCACCGCCAGACTGCAC-3'

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

[illegible]

FIG. 48A

FIG. 48C

FIG. 48D

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1201 ATACGATTTA GGTGACACTA TAGATAACAT CCACCTTTGCC TTTCTCTCCA CAGGTGTCCA CTCCAGGTC CAACCTGCACC TCGGTCTCTAT CGATTGAATT
TATGCTAAAT CCACCTGTGAT ATCTATTGTA GGTGAACCG AAGAGAGGT GTCCACAGGT GAGGGTCCAG GTTGACTGCG AGCCAGATA GCTAACTTAA
seq from PRK6G425VH: Cla-AvrII^

1301 CCACCATGGG ATGGTCATGT ATCATCCTTT TTCTAGTAGC AACTGCAACT GGAGTACATT CAGAAGTTCA GCTAGTGCAG TCTGGCGGTG GCCTGTGCA
GGTGGTACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTTGA CCTCATGTAA GTCTTCAAGT CGATCACGTC AGACCGCCAC CGGACCACGT
E V Q L V Q S G G L V Q

1

1401 GCCAGGGGCG TCACTCCGTT TGTCTGTGCG AGCTTCTGCG TACTCTTCT CGAGTCACTA TATGCACTGG GTCCGTGAGG CCCGGGTAA GGCCTGGAA
CGGTCCCGCG AGTGAGGCAA ACAGGACCG TCGAAGACCG ATGAGGACCG GTCTAGTATGAT ATACGTGACC CAGGAGTCC GGGGCCCCATT CCGGACCTT
14 P G G S L R L S C A A S G Y S F S S H Y M H W V R Q A P G K G L E

FIG. 48E

FIG. 48F

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scrFI      hgiAI/aspHI      hlnPI
mvaI      nlaIV      nari
ecorII     bsp1286
econI
daav      kasI
bstNI     hlnII/acyI      bmyI      mspI
bsII      hgiCI      cacBI      hpall
apyl{dcm+} haelI      bnu4HI      scrFI
fnu4HI     bsoFI      nciI
bscFI      acil apall/snoI      dsav
bbvI       ahalI/bsaHI      acilI alw44I/snoI cauII      scfI
1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCC GAACCGGTGA CGGTGTCGTG GAACTCAGGC GCCCTGACCA GCGGCGTGCA CACCTTCCG GCTGTCTTAC
GACCCGACGG ACCAGTTCTT GATGAAGGGG CTGGCCACT GCCACAGCAC CTTGACTCCG CGGACTGGT GCGCCGACGT GTGGAAGGCG CGACAGGATG
147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q

fnu4HI     nlaIV      hgiCI      tfII
bscFI      bani      hinfi
rmaI       bsp1286      meel      maeII
bspl286    bfaI aluI bsp1286      bmyI
maeIII     hphI      bmyI      bbvI      bmyI
hphI       bmyI      mnlI      bbvI      bmyI
1901 AGTCTCAGG ACTCTACTCC CTCAGCAGCG TGCTGACTGT GCCCTCTAGC AGCTTGGCA CCCAGACCTA CATCTGCAAC GTGATCACA AGCCAGCAA
TCAGAGTCC TGAGATGAGG GATGCTCGC ACCACTGACA CCGGAGATCG TCGAACCGT GGTCTGGAT GTAGACGTG CACTTAGTGT TCGGTCGTT
181 S S G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N

abdl/eam1105I
sau96I
avaII

scrFI      mvaI      asuI
ecorII     dsav
bstNI      nlaIV      mboII
bsaJI      bsmFI      bpuAI
apyl{dcm+} bbsI mnlI
2001 CACCCAGGTG GACAAGAAAG TTGAGCCCA ATCTTGTGAC AAAACTCACA CATGCCACCC GTGCCAGCA CCTGAACCTCC TGGGGGACC GTCAGTCTTC
GTGTTCCAC CTGTTCTTTC AACTCGGGT TAGAACACTG TTTTGTGATGT GTACGGGTG CACGGGTGCGT GGACTTGAGG ACCCCCTGG CAGTCAGNAG
214 T K V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F

```

FIG. 48G

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```

sau96I      sau3AI      avalI      nlaIII
nlaIV
mspI
hpaII
scrFI
ncII
dsav
sau3AI      avalI      nlaIII
mboI/ndelI[dam-]      nspI
nlaIII      cauII      mnII      nspHI
rcal dpmI[dam+]      ddel      mslI
mnII      dpmII[dam-]      eco8II      maelII
mslI      bspHI[dam-]      asuI      bsu36I/mstII/sauI
earI/ksp632I      bsaJI      mslI      bspHI[dam-]      asuI      bsu36I/mstII/sauI
CTCTTCCCCC      CAAACCCAA      GGACACCTC      ATGATCTCCC      GGACCCCTGA      GGTACATGC      GTGTGGTGG      ACCTGAGCCA      CGAGACCCCT      GAGGTCAAGT
2101      CTCTTCCCCC      CAAACCCAA      GGACACCTC      ATGATCTCCC      GGACCCCTGA      GGTACATGC      GTGTGGTGG      ACCTGAGCCA      CGAGACCCCT      GAGGTCAAGT
GAGAAGGGGG      GTTTGGTT      CCTGTGGAG      TACTAGAGGG      CCTGGGGACT      CCAGTGACG      CACCACCACC      VCVVDVSH      EDPEVKF
247      LFPKPKD      TLMISRTPE      VTCVVDVSH      EDPEVKF

```

2201 TCAACTGGTA CGTGGAGCGG GTGGAGGTGC ATAATGCCAA GACAAGCCG CGGAGGAGC AGTACAACAG CACGTACCGT GTGTACCGT TCCTACCGT

281 N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V

2301 CCTGCACCAG GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGGTCTCCA ACAAGCCCT CACAGCCCC ATCGAGAAA CCATCTCCAA AGCCAAAGG

314 L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G

2201 TCAACTGGTA CGTGGAGCGG GTGGAGGTGC ATAATGCCAA GACAAGCCG CGGAGGAGC AGTACAACAG CACGTACCGT GTGTACCGT TCCTACCGT

281 N W Y V D G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V

2301 CCTGCACCAG GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGGTCTCCA ACAAGCCCT CACAGCCCC ATCGAGAAA CCATCTCCAA AGCCAAAGG

314 L H Q D W L N G K E Y K C K V S N K A L P A P I E K T I S K A K G

FIG. 48H

FIG. 48I

[illegible]

FIG. 48J

FIG. 48K

FIG. 48L

FIG. 48M

FIG. 48N

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```

151 V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S T
      rsal      mnlI      maelII bsaJI      maelIII      fnu4HI
      csp6I     bslI      maelIII bsaJI      maelIII      ddel bsoFI
4101 AGTACAGTGG AAGGTGGATA ACGCCCTCCA ATCGGGTAAC TCCAGGAGA GTGTCACAGA GCAGGACAGC AAGGACAGCA CCTACAGCCT CAGCAGCACC
      TCCAGTCACT TCCACCTAT TCGGGGAGGT TAGCCCATG TAGCCCATG AGGTCCTCT CACAGTGTCT CGTCCTGTCG TTCCTGTGCT GGATGTGGA GTCTGTGTCG
151 V Q W K V D N A L Q S G N S Q E S V T E Q D S K D S T Y S L S S T
      sstI
      sacI
      hgiI
      hgiAI/aspHI
      eciI36II
      bspI286
      bsiHKAI
      bmyI
      ddel cac8I
      haeIII/palI
      sau96I aluI
      asuI banII
      hphI      ecoli09I/draII      maelII      aluI
4201 CTGACGCTGA GGAAGCAGA CTACGAGGAA CACAAAGTCT ACGGCTGCGA AGTCACCAT AGTCACCAT CAGGGCTGA GCTCGCCCGT CACAAAGAGC TTCAACAGGG
      GACTGCGACT CGTTTCGTCT GATGCTCTT GTGTTTCAGA TCGGAGCGCT TCAGTGGGTA GTCCCGGACT CGAGGGGCA GTGTTTCTCG AAGTTGTCCC
184 L T L S K A D Y E K H K V Y A C E V T H Q G L S S P V T K S F N R G
      sau96I
      accI      cac8I      hphI      maelIII      aluI
      acII      haeIII/palI
      fnu4HI      asuI
      bsoFI      nlaIII
      sfiI      styI
      aluI      haeIII/palI
      hindIII      bglI      ncoI
      tru9I      eaeI      dsal
      mseI      cfrI      bsaJI
4301 GAGAGTGTTA AGCTTGCCCG CCATGGCCCA ACTGTGTTAT TGCAGCTTAT AATGCTTACA AATAAGCAA TAGCATCACA AATTCACAA ATAAAGCATT
      CTCTCACAAT TCGAACCGGC GGATCCGGGT TGAACAATA ACGTCGAATA TTACCAATGT TTATTTGTTT ATCGTAGTGT TTAAGTGT TATTTCGTAA
218 E C O

```

FIG. 480

FIG. 48P

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682760 4405566

```

nlaIII
styl
ncol
bsli dsal
acii bsaji
4701 ATCTCAATTA GTCAGCAACC ATAGTCCCGC CCCTAACTC CGCCAGTTC CGCCATTCT CGGCCCATG GCTGACTAAT
TAGAGTTAAT CAGTCGTTGG TATCAGGGCG GGGATTGAG CGGGTCAAG GCGGTAAGA GCGGGGTAC CGACTGATTA

acii
bsmFI
4801 TTTTATTAT TATCAGAGG CCGAGGCGC CTCGGCTCT GAGTATTCC AGAGTCTT AGGAGCTT TTTGGAGCC TAGGCTTTG CAAAAGCTG
AAAAAATAA ATAGTCTCC GGCTCCGGG GAGCCGAGA CTCGATAAG TCTTCATCAC TCCTCCGAA AACCTCCG ATCCGAAAC GTTTTCGAC
start puc118^

fnu4HI
bsoFI
bglI
sfiI
haeIII/palI
mnli mnli ddeI
haeIII/palI bsaji mnli alul
mnli bsaji acii haeIII/palI
4801 TTTTATTAT TATCAGAGG CCGAGGCGC CTCGGCTCT GAGTATTCC AGAGTCTT AGGAGCTT TTTGGAGCC TAGGCTTTG CAAAAGCTG
AAAAAATAA ATAGTCTCC GGCTCCGGG GAGCCGAGA CTCGATAAG TCTTCATCAC TCCTCCGAA AACCTCCG ATCCGAAAC GTTTTCGAC
start puc118^

fnu4HI
haeIII/palI
mcrI
eagI/xmaIII/ecI XI
eaeI
notI
bsrBI bsoFI
taqI cfrI
xhoI fnu4HI tru9I
paer7I bsiEI pacI
avaI bsoFI msel tru9I bsh1236I msel
mnli acii acii msel bssHII swaI sse8387I alul
4901 TTACCTCGAG CGGCCGCTTA ATTAAGGCGC GCCATTAA TCTGCAGGT AACAGCTGG CACTGGCCGT CGTTTACAA CGTCGTGACT GGGAAACCC
AATGGACCTC GCGGGCGAAT TAATTCGGG CGGTAAATTT AGGACGTCCA TTGTGCAACC GTGACCGCA GCAAAATGTT GCAGCACTGA CCCTTTTGGG
^linearization linker inserted into HpaI site

scrFI
mvaI
ecorII
dsav
bstNI
apyI[dcM+]
bsrI
maeII maeIII
bsaji

```

FIG. 48Q

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```

          sau3AI
mboI/ndeII(dam-)
dpnI(dam+)
          sau96I
          haeIII/palI
          asuI
          mnlI acII
          pmlI/bspCI
          mboII cac8I mcrI
          earI/ksp632I bslEI
          CGAAGAGGCC CGCACCAGATC GCCCTTCCCA ACAGTTGCGT
          GCTTCTCCG GCGTGGCTAG CGGAAGGGT TGTCACACGCA
          cac8I
          aluI
          pvuII
          nspBII
          cac8I
          fokuI
          fnu4HI
          bsoFI
          bbvI
          tru9I
          msel
          maeIII
          CAACTTATC GCCTTGCAGC ACATCCCCC TTGCGCCAGT GCGGTAATAG
          CGGAACGTCG TGTAGGGGG AAGCGGTGCA CCGCATTATC
          hinPI
          hhaI/cfoI
          nlaIV
          narI
          kasi
          hinII/acyI
          hgiCI
          haeII
          acII
          bani
          sfaNI
          ahaII/bsaHI
          bglI
          AGCCTGAATG GCGAATGGCG CCGATGCGG TATTTCTCC TTACGCATCT GTGGGTATT TCACACCGCA TAGTCAAG CAACCATAGT ACGGCCCCCTG
          TCGGACTTAC CGCTTACCGC GGACTAGGCC ATAAAGAGG AATGCGTAGA CACGCCATAA AGTGTGGCGT ATGCAGTTTC GTTGGTATCA TCGCGGGGAC
          hinPI
          thal
          fnuDII/mvni
          bstOI scfI
          bsh1236I
          rsaI hhaI/cfoI
          csp6I bslI
          acII
          fnu4HI
          bsoFI
          thal
          fnuDII/mvni
          bstOI
          hinPI
          hhaI/cfoI
          hhaI/cfoI
          hinPI haeII
          hhaI/cfoI bsrBI
          haeII maeI acII
          maeIII bbvI maeIII
          cac8I bfaI cac8I
          mboII
          GGTACGCG AGCGTGACCG CTACACTTGC CAGCGCCCTA GCGCCCGCTC CTTTCGCTTT CTTCCTTCC
          ATCGCCGCGT AATTCGCGCC GCCACACCA CCAATGCGG TCGCACTGGC GATGTGAACG GTCGCGGAT CCGCGGCGAG GAAAGCGAA GAAGGNAAG

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FIG. 48R

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5301 TTTCTCGCCA CGTTGCGCGG CTTTCCCGCT CAACTCTCTAA ATCGGGGGCT CCCTTAGGG TTCCGATTTA GTGCTTTAGC GCACCTCGAC CCCAAAAAAC
 AAAGAGCGGT GCAAGCGGCC GAAAGGGGCA GTTCGAGATT TAGCCCCCGA GGGAAATCCC AAGCTAAAT CACGAATGC CGTGGAGCTG GGGTTTTTGG
 nlaIV hgiJII bsp1286 bmyI baniI nlaIV
 mspI hpaII naeI cfr101/bsrFI aluI
 maeII cac8I
 maeII haeIII/palI
 draIII sau96I
 bsaAI asuI
 hphI
 5401 TTGATTGGG TGATGGTTCA CGTAGTGGG CATCGCCCTG ATAGACGGTT TTTCGCCCTT TGACGTTGGA GTCCACGTTT TTTAATAGTG GACTCTGTT
 AACTAAACC ACTACCAAGT GCATCACCG GTAGCGGGAC TATCTGCCAA AAAGCGGAA ACTGCAACCT CAGGTGCAAG AAATTATCAC CTGAGAACAA
 maeII pleI
 drdI hinfI maeII
 tru9I mseI
 pleI hinfI
 5501 CCAAACTGA ACAACACTCA ACCCTATCTC GGGCTATTCT TTGATTTAT AAGGGATTT GCGGATTTTC GCCTATTGGT TAAAAAATGA GCTGATTAA
 GGTTCACCT TGTGTGAGT TGGGATAGAG CCCGATAGAG AACTAAATA TTCCCTAAAA CGGCTAAAGC CGGATAACCA ATTTTACT CGACTAAT
 bslI
 bslI avai
 haeIII/palI
 aluI mseI
 tru9I mseI
 5601 CAAAAATTA ACGCGAATTT TAACAAATA TTAACGTTTA CAATTTTATG GTGCACCTCT AGTACAATCT GCTCTGATGC CGCATAGTTA AGCCAACTCC
 GTTTTAAAT TGCCTTAA ATTGTTTAT AATTGCAAT GTTAAATATC CAGGTGAGAG TCATGTTAGA CGAGACTACG CGGTATCAAT TCGGTTGAGG
 thal fnuDII/mvnl maeII psp1406I
 tru9I apoI tru9I
 mseI bstUI mseI
 apoI bsh1236I sspI mseI
 hgiAI/aspHI
 bsp1286
 bsiHKA
 bmyI ddeI
 apaLI/snoI rsaI
 alw44I/snoI csp6I
 sfaNI
 sfaNI
 fnu4HI
 bsoFI
 tru9I
 mseI
 acII
 5701 GCTATCGCTA CGTACTGGG TCATGGCTGC GCCCGACAC CCGCCACAC CCGCTGACG GCTTGTCTGC TCCCGGCATC CGCTTACAGA
 CGATAGCGAT GCACTGACCC AGTACCAGC CGGGGCTGTG GCGGACTGCG GCGGACTGCC CGAACACAGC AGGGCCGTAG CGCAATGTCT
 hinPI
 hhaI/cfoI
 thal
 fnuDII/mvnl
 bstUI
 nspBII bsh1236I
 acII hgaI drdI
 acII
 maeIII
 maeII bsrI nlaIII hhaI/cfoI
 bsaAI tth111I/aspI bbvI
 dsav foki
 cauli acII
 mspI
 hpaII
 scrFI
 nciI
 sfaNI

FIG. 48S

5801
 ATGCGGATAT GTAAGTTTAT ACATAGGCGA AATATATCCAA TTACAGTACT ATTATTACCA AAGAATCTGC AGTCCACCGT GAAAGCCCC TTACACGCG CTTGGGGAT AAACAAATAA
 5901
 TAGGCTTATT TTTATAGGTT AATGTCATGA TAATATAGGT TTTCTAGACG TCAGGTGCGA CTTTCGGGG AAATGTGGC GGAACCCCTA TTTGTTTATT
 6001
 TTTCTAATA CATTCAAATA TGTATCCGCT CATGAGACAA TAACCTGAT AATGCTTCA ATAATATGA AAAGGAAGA GTATGAGTAT TCAACATTTC
 6101
 CGTGTGCGCC TTATTCCCTT TTTTGGCGCA TTTTGCCTTC CTGTTTTTGC TCACCCAGAA ACCTGGTGA AAGTAAAGA TGCTGAAGT CAGTTGGGTG
 GCACAGCGG AATAAGGGA AAAACGCCGT AAAACGGNAG GACAAAACG AGTGGTCTT TGCACCACT TTCATTTTCT ACGACTTCTA GTCAACCCAC

FIG. 48T

[illegible]

FIG. 48U

hinPI mspI
 hhal/cfoI hpaII
 mstI aluI scrFI tru9I
 avIII/fspI bsrI maeI
 maeII psp1406I maeI asei/asnI/vspI
 fnu4HI bsoFI cac8I bsrDI
 mslI sfanI bsvI
 maeIII bsrDI
 6601 CGACGAGCGT GACACACGGA TGCCAGCAGC AATGGCAACA ACSTTGGCGA AACTATTAAAC TGCGGAACTA CTACTCTAG CTCCCGGCA ACAATTAAATA
 GCTGCTCGCA CTGTGGTGCT ACGGTCTGCTG TTACCGTTGT TGCACGCGGT TTGATAATTG ACCGCTTGAT GAATGAGATC GAAGGCGCGT TGTTAATTAT
 bglI mspI
 sau96I cac8I
 haeIII/palI
 hinPI asuI mspI bsmAI
 hhal/cfoI hpaII nlaIV hphI
 6701 GACTGGATGG AGCGGATAA AGTTGCAGGA CCACCTTCTGC GCTCGGCCCT TCCGGCTGCG TGTTTTATTG CTGATAAATC TGGAGCCGGT GAGCGTGGET
 CTGACCTACC TCCGCTATT TCAACGTCCT GGTGAAGAGC CGAGCGGGGA AGCCCGACCG ACCAAATAAC GACTATTAG ACCTCGGCCA CTGCGACCCA
 acII fnu4HI haeIII/palI
 thalI fnuDII/mvnI bsoFI sau96I
 bstUI bsvI nlaIV
 bsh1236I bsrDI bsrI asuI
 6801 CTGCGGTAT CATTCAGCA CTGGGGCCAG ATGGTAAGCC CTCCCGTATC GTAGTTATCT ACACGACGGG GAGTCAGGCA ACTATGGATG AACGAAATAG
 GAGCGCCATA GTACGTCGT GACCCCGGTC TACCATTCCG GAGGCGATAG CATCAATAGA TGTGCTGCCC CTCAGTCCGT TGATACCTAC TTGCTTTATC
 ddeI
 sau3AI nlaIV
 mboI/ndeII[dam-]
 dpnI[dam+] hgiCI tru9I
 dpnII[dam-] banI mnlI maeI
 6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATTTG TAAGCTGTCAG ACCAAGTTTA CTCATATATA CTTTAGATTG ATTTAAACT TCATTTTAA
 TGCTAGCGA CTCTATCCAC GGAGTGACTA ATTCGTAACC ATTGACAGTC TGTTCAAT GAGTATATAT GAAATCTAAC TAAATTTGA AGTAAAAAT
 rmaI sau3AI
 maeI mboI/ndeII[dam-]
 sau3AI mboI/ndeII[dam-]
 dpnI[dam+] dpnI[dam-]
 dpnII[dam-] dpnII[dam-]
 tru9I bstVI/xhoII alwI[dam-]
 maeI alwI[dam-] bstVI/xhoII
 ahalII/draI bfaI mboII[dam-]
 7001 TTTAAAGGA TCTAGGTGAA GATCCCTTTT GATAATCTCA TGACCAAAAT CCCTTAACGT GAGTTTCGT TCCACTGAGC GTCAGACCCC GTAGAAAGA
 AAATTTCTCT AGATCCACTT CTAGGAAAAA CTATTAGAGT ACTGGTTTGA GGAATGCA CTCAAAGCA AGGTGACTCG CAGTCTGGG CATCTTTCT

FIG. 48V

FIG. 48W

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66E760"4F09EE60

```

scrFI      mvaI      ecorII     dsav      bstNI      haeII      hinPI      hhaI/cfoI
7501 TGAGCATTGA GAAAGGCCA CGCTTCCGA AGGAGAAAG GCGGACAGGT ATCCGGTAAG CGGCAGGCTC GGAACAGGAG AGCGCAGCAG GGAGCTTCCA
ACTCGTAACT CTTTCGGGT GCGAAGGGCT TCCCTCTTTC CGCCTGTCCA TAGGCATTC GCCGTCCAG CCTTGCTCTC TCCTCGAAGGT

scrFI      mvaI      ecorII     dsav      bstNI      haeII      hinPI      hhaI/cfoI      bssSI      hinPI      mnlI      hhaI/cfoI      aluI      apyI[dcM+]
7601 GGGGAAACG CTTGGTATCT TTATAGTCTT GTCCGGTTTC GCCACCTCTG ACTTGAGCGT CGATTTTGTG ATGCTCGTC AGGGGGCGCG AGCCTATGGA
CCCCCTTTCG GGACCATAGA AATATCAGGA CAGCCCAAAG CGGTGAGAG TGAACTCGCA GCTAAAACA CTACGAGCAG TCCCCCGCGC TCGGATACCT

scrFI      mvaI      ecorII     dsav      bstNI      haeII/palI      haeIII/palI      nlaIV      acII
7701 AAAACGCCAG CAACGGCCG TTTTACGGT TCCTGGCCCT TTGCTGCCCT TTTGCTCACA TGTCTTTCC TCGGTTATCC CCTGATTCTG TGGATAACCG
TTTTCGGCTC GTTGGCCCGG AAAATGCCA AGGACCCGGA AACGACCGGA AAACGAGTGT ACAGAAAGG ACCTAATAGG GGACTAAGAC ACCTATTGGC

scrFI      mvaI      ecorII     dsav      bstNI      haeII/palI      haeIII/palI      nlaIV      acII
7801 TATTACCGCC TTTGAGTGAG CTGATACCGC TCGCGCGCAG CGAACGACCG AGCGAGCGGA GTCAGTAGGC GAGGAGCGCG AGAGCGGCCC AATACGCAAA
AATATGGCGG AAATCACTC GACTATGCGC GCTTGCTGSC TCGGCTCGCT CAGTCACCTG CTCCTTCGCC TTCTCGCGCG TTATCGGTTT

```

FIG. 48X

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```

thai
fndDII/mvnI
bstUI
bsh1236I
hinPI
hhaI/cfoI
thai
fndDII/mvnI          cac8I
bstUI haeIII/palI    aluI
bsh1236I              tru9I pvuII
mnlI eaeI tfII aseI/asnI/vspI
aciI cfrI hinfI mseI nspBII
7901 CCGCCTCTCC CCGCGGTTG GCGGATTTCAT TAATCCAGCT GGCAGACACAG GTTCCCGAC TGGAAAGCGG GCAGTGAGCG CAACGCAATT AATGTGAGTT
GGCGGAGAGG GCGCGGCAAC CGGCTAAGTA ATTAGGTGCA CCGTGTGTC CAAGGGCTG ACCTTTCGCC CGTCACTCGC GTTGGGTTAA TTACACTCAA
tru9I mseI maeIII
hinPI hhaI/cfoI aseI/asnI/vspI
cac8I aciI
bseI
8001 ACCTCACTCA TTAGGCACCC CAGGCTTTAC ACTTTATGCT TCCGGCTCGT ATGTTGTGTG GAATTGTGAG CGGATAACAA TTTCACACAG GAAACAGCTA
TGGAGTGAGT AATCCGTGGG GTCCGAATG TGAATACGA AGGCCGAGCA TACAACACAC CTTAACACTC GCCTATTGTT AAAGTGTC CTTTGTGAT
mspI hpaII
nlaIV bstNI
hgiCI apyI[dcmt+]
banI bsaJI
mnlI

```

FIG. 48Y

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```

      tru9I
      mseI
      asel/asnl/vspi
      xmni
      nlaII
      asp700
8101 TGACCATGAT TACGAATTAA
      ACTGGTACTA ATGCTTAATT

>length: 8120

aatII(GACGTC):      1690 5947
acc65I(GGTACC):    2969 3967 4529
      823 1039 2738 4237
accI(GTMKAC):      217 229 238 250 260 271 317 422 454 485 574 1385 1795 1871 2248 2250 2758 2982
      3167 3179 3188 3200 3210 3221 3267 3372 3404 3449 3686 3949 4021 4318 4542 4727
      4739 4748 4760 4770 4781 4827 4910 4914 5070 5127 5153 5166 5203 5217 5220 5248
      5275 5680 5699 5741 5751 5790 5979 6026 6125 6234 6311 6355 6476 6522 6713 6804
      7166 7175 7310 7420 7541 7560 7687 7715 7806 7827 7834 7877 7901 7911 7967 8070
      see hinII
acyI
aflII/bfII(CTTAAG): 786
aflIII(ACRYGT):     932 7758
ageI(ACCGGT):       1833
      988 1690 1858 5117 5947 6329
ahaII/bsaHI(GRCGYC): 696 4935 6290 6982 7001
      5 44 332 386 390 753 1097 1165 1370 1431 1951 2603 2751 2784 3282 3336 3340
ahdI/eam1105I(GACNNNNNGTC): 2087 6865
      3562 3566 3676 3733 3792 4270 4288 4311 4344 4554 4842 4896 4954 5047 5333 5590
      5803 5822 6516 6579 6679 7200 7457 7593 7819 7937 8096
      1876 5651 6198 7444
alw44I/snoI(GTGCAC):

```

FIG. 48Z

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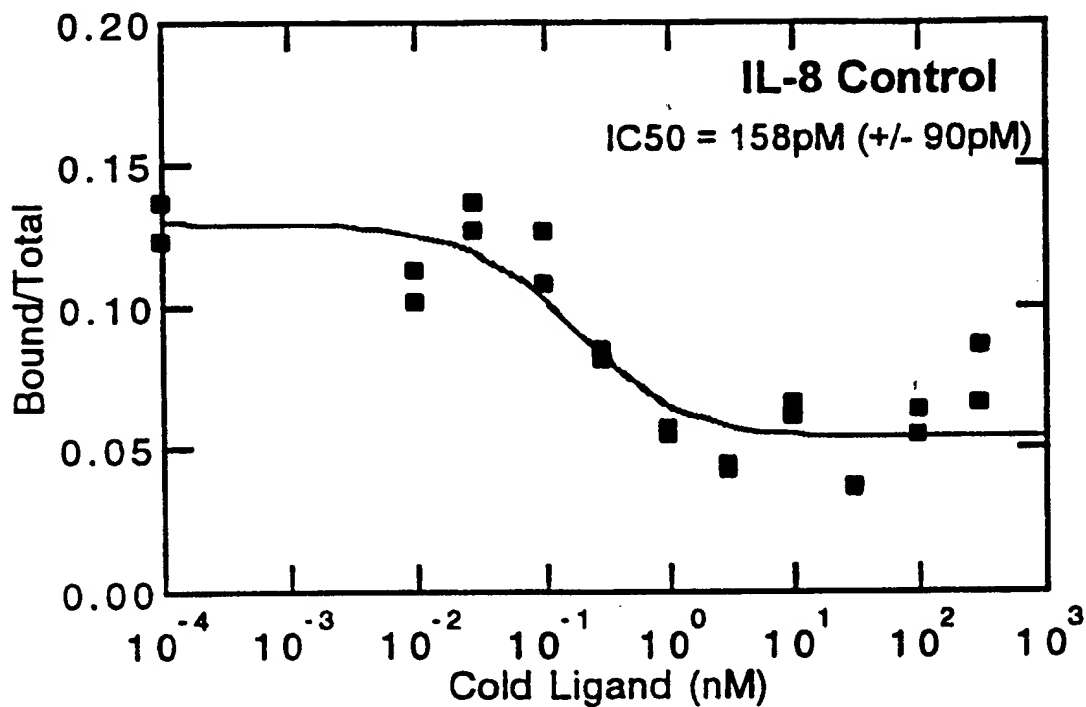


FIG. 49A

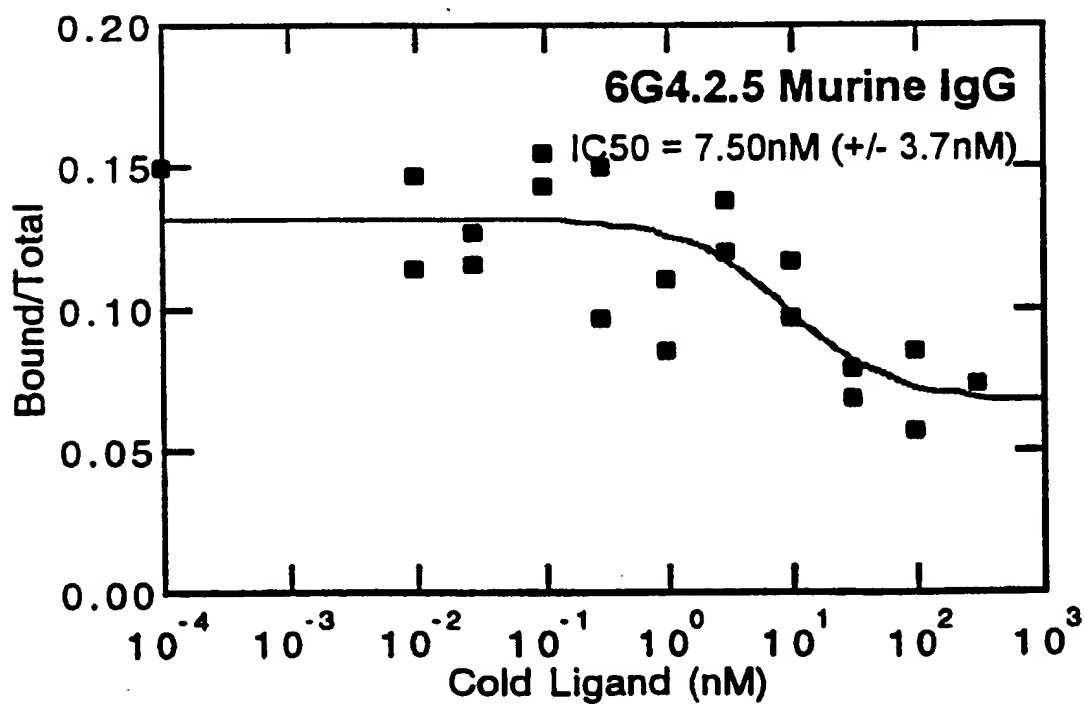


FIG. 49B

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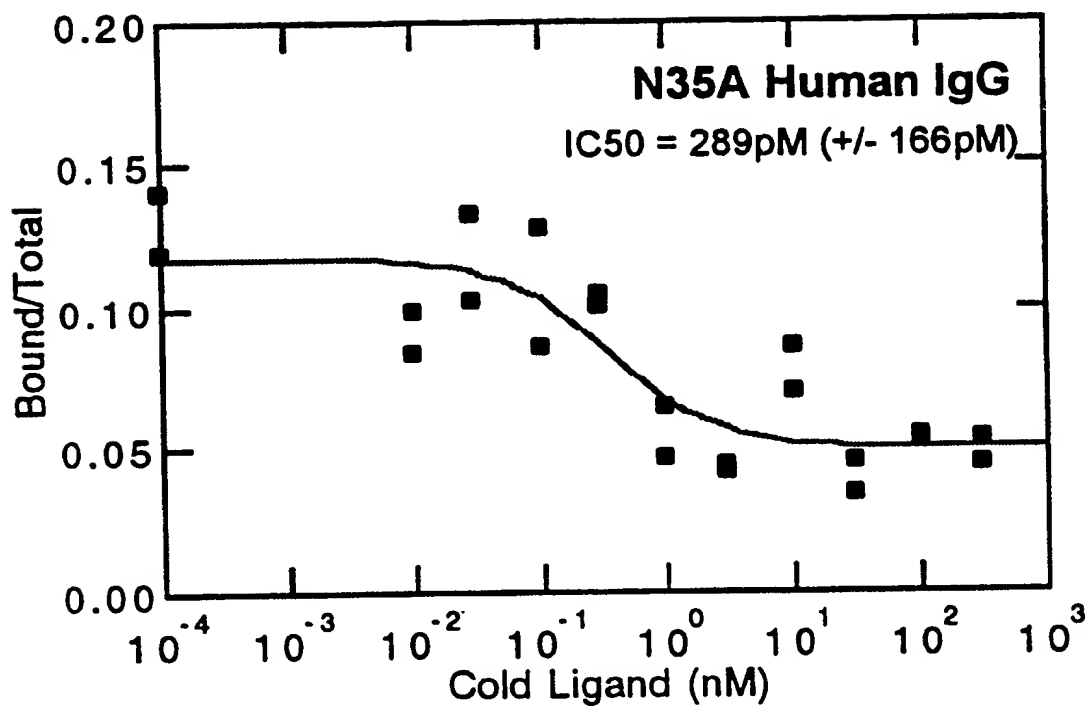


FIG. 49C

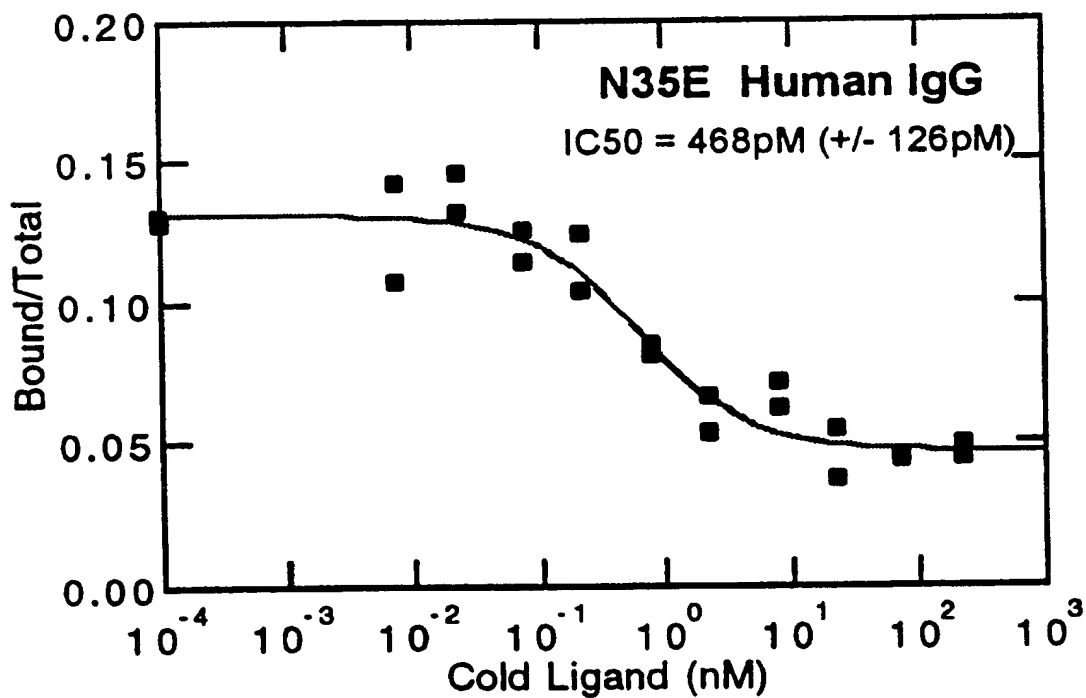


FIG. 49D

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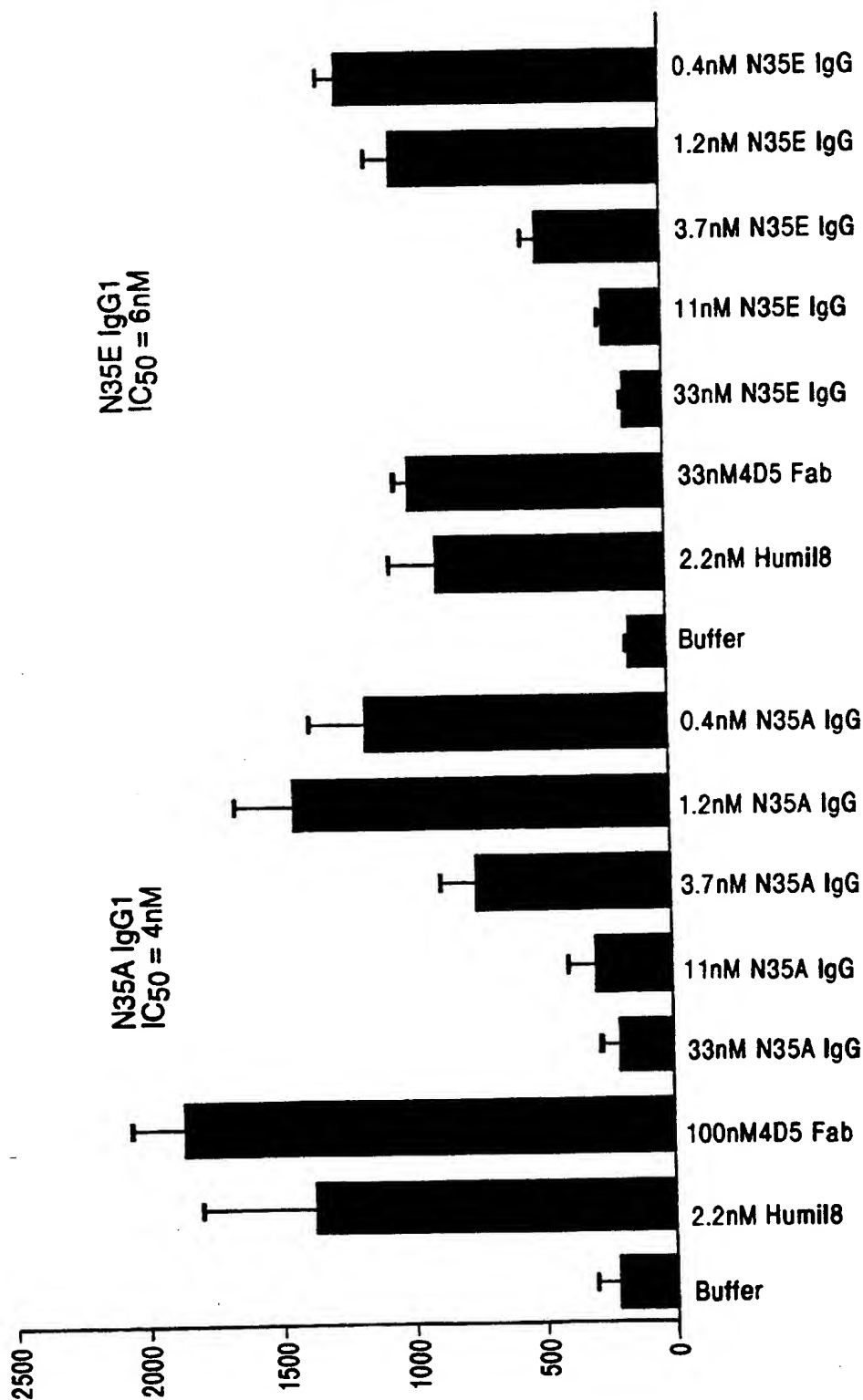


FIG. 50A

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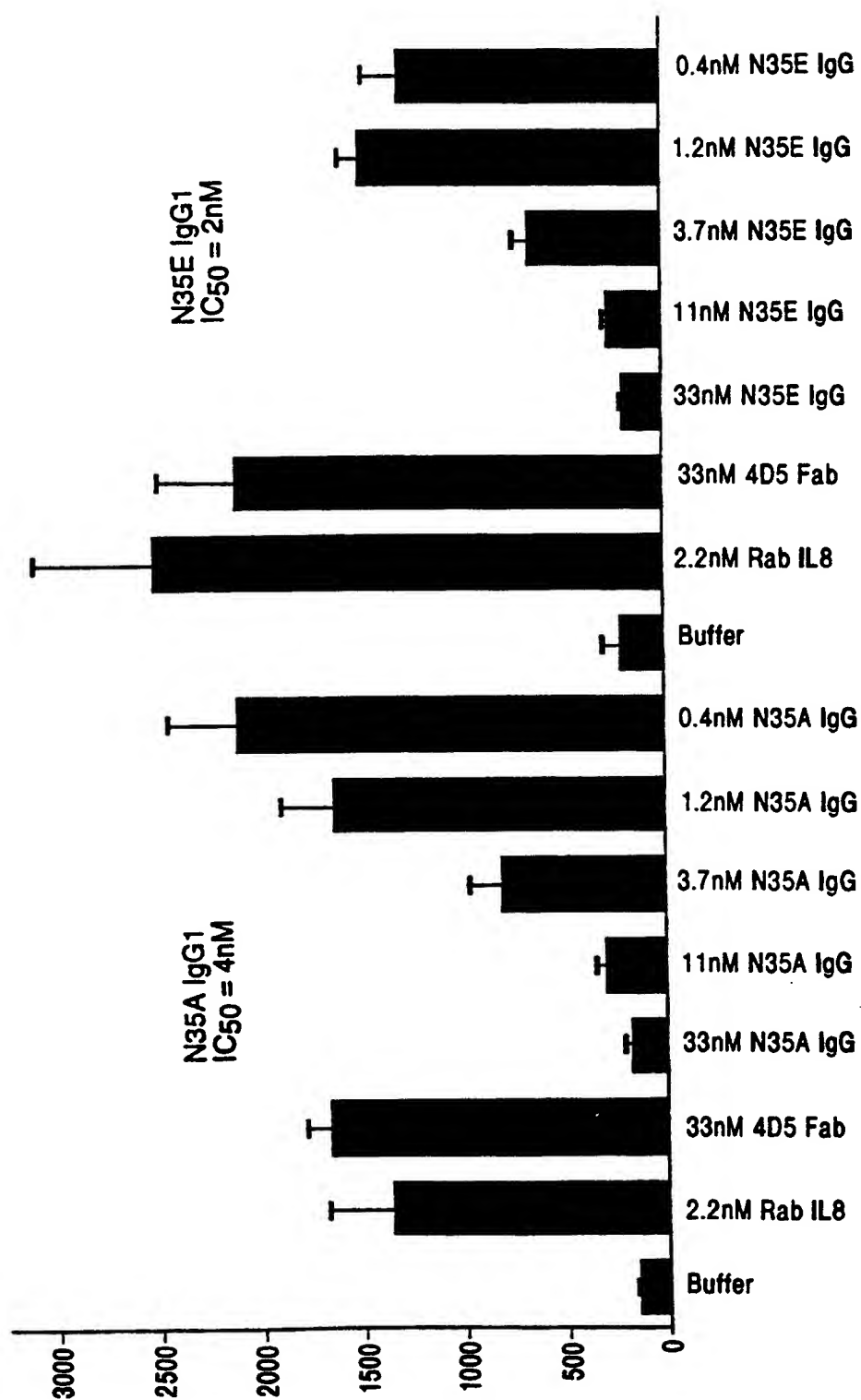
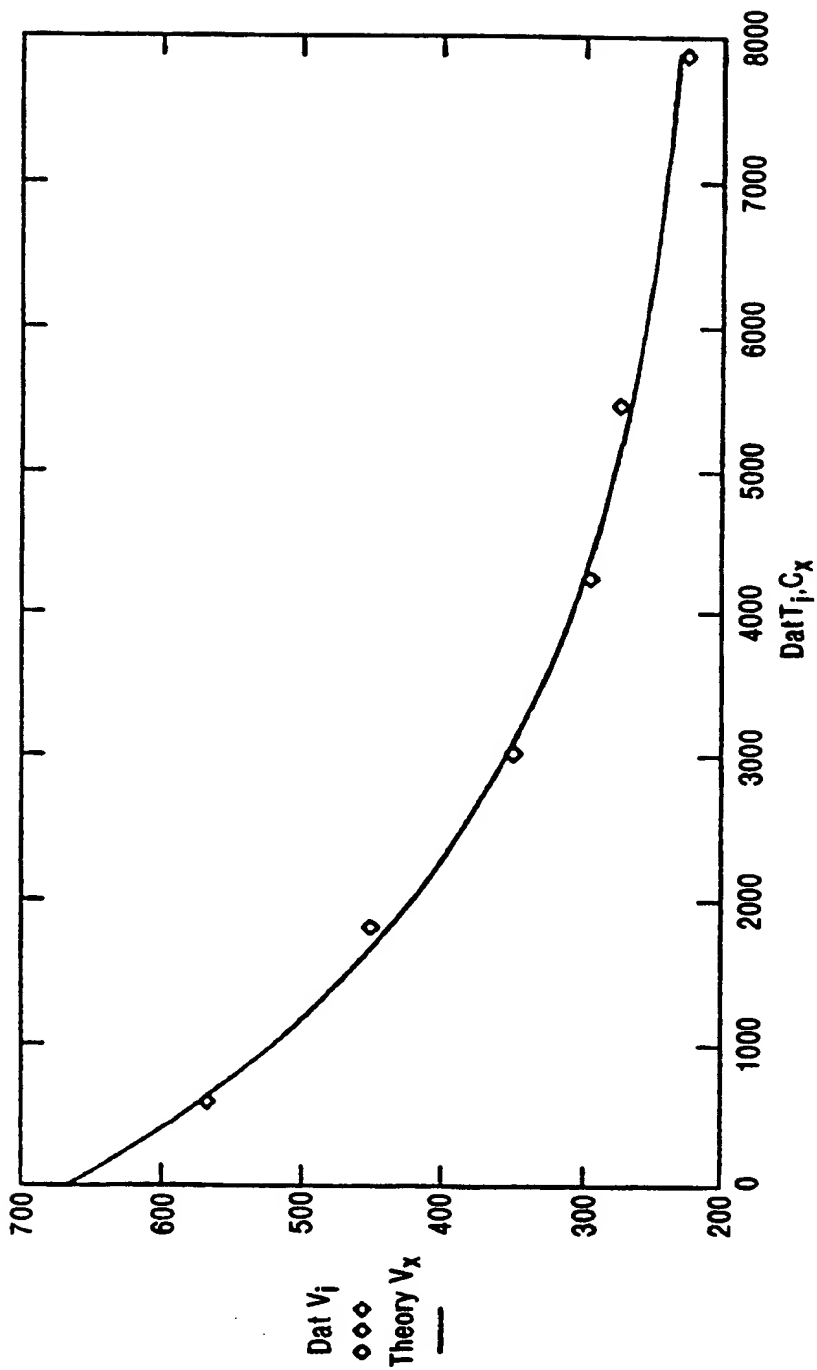


FIG. 50B



Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.IgG1

SAMPLE	ka	kd	Kd
Murine 6G4.2.5 IgG2a	8.3x10 ⁵	2.9x10 ⁻⁴	350pM
6G4V11N35A-IgG1	8.7x10 ⁵	7.7x10 ⁻⁵	88pM
6G4V11N35E-IgG1	3.0x10 ⁶	1.4x10 ⁻⁴	49pM

FIG. 51

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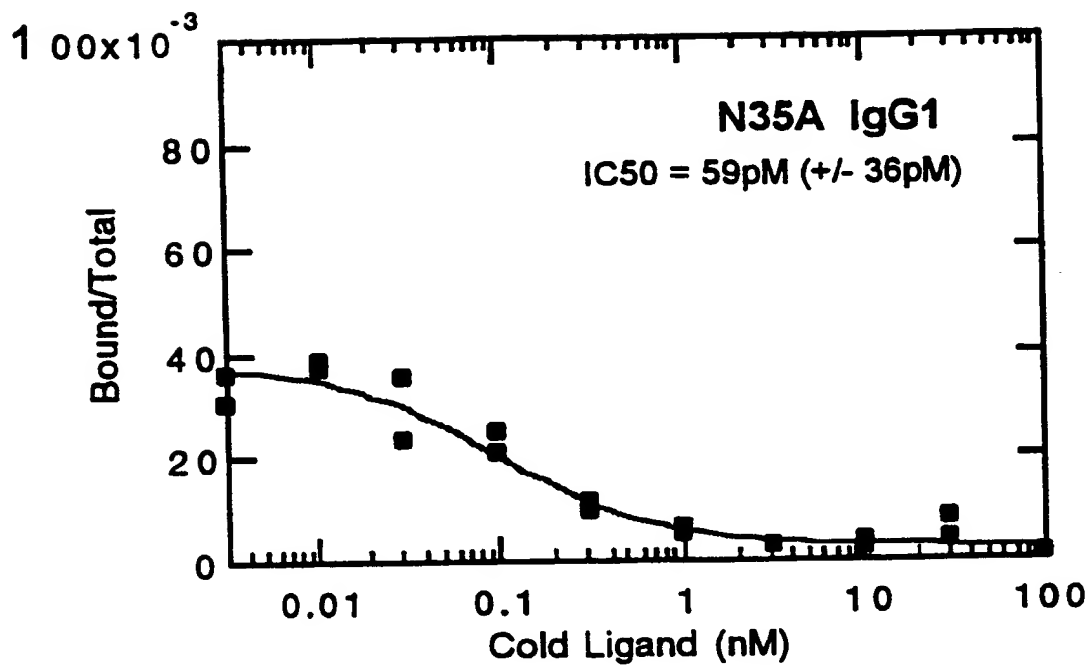


FIG. 52A

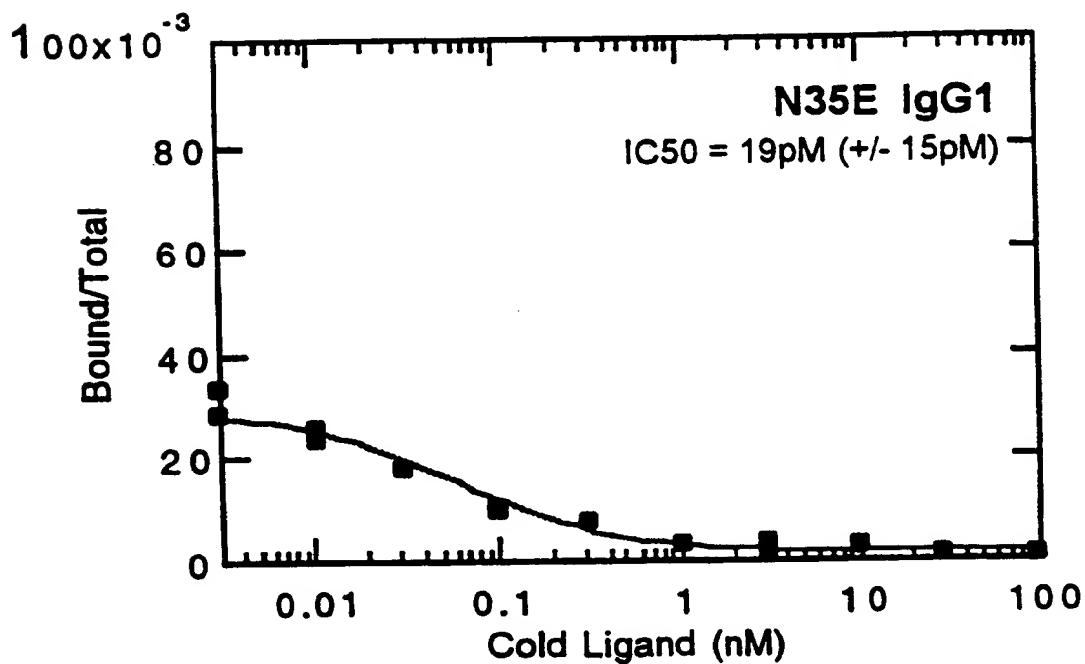


FIG. 52B

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781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA
 TTTTCCCAT A GATCTCCAAC TCCACTAAAA TACTTTTTTCT TATAGCGTAA AGAAGAACGT
 -1 M K K N I A F L L A
 841 TCTATGTTTCG TTTTTCCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA
 -11 S M F V F S I A T N A Y A E V Q L V Q S
 901 GCGGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC
 CCGCCACCGG ACCACGTCGG TCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG
 8 G G G L V Q P G G S L R L S C A A S G Y
 961 TCCTTCTCGA GTCACTATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTTCCC GGACCTTACC
 28 S F S S H Y M H W V R Q A P G K G L E W
 1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA
 48 V G Y I D P S N G E T T Y N O K F K G R
 1081 TTTACTTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA
 68 F T L S R D N S K N T A Y L Q M N S L R
 1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC
 88 A E D T A V Y Y C A R G D Y R Y N G D W
 1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC
 AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG
 108 F F D V W G Q G T L V T V S S A S T K G
 1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC
 128 P S V F P L A P S S K S T S G G T A A L
 1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC
 CCGACGGACC AGTTCTTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG
 148 G C L V K D Y F P E P V T V S W N S G A
 1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTA CTCCCTC
 GACTGGTCCG CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG
 168 L T S G V H T F P A V L Q S S G L Y S L
 1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG
 TCGTCGCACC ACTGGCACGG GAGGTGCTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC
 188 S S V V T V P S S S L G T Q T Y I C N V
 1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA
 TTAGTGTTTCG GGTCTGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT
 208 N H K P S N T K V D K K V E P K S C D K
 1561 ACTCACACAT GCCCGCCGTGA
 TGAGTGTGTA CGGGCGGCACT
 228 T H T C P P O

FIG. 53

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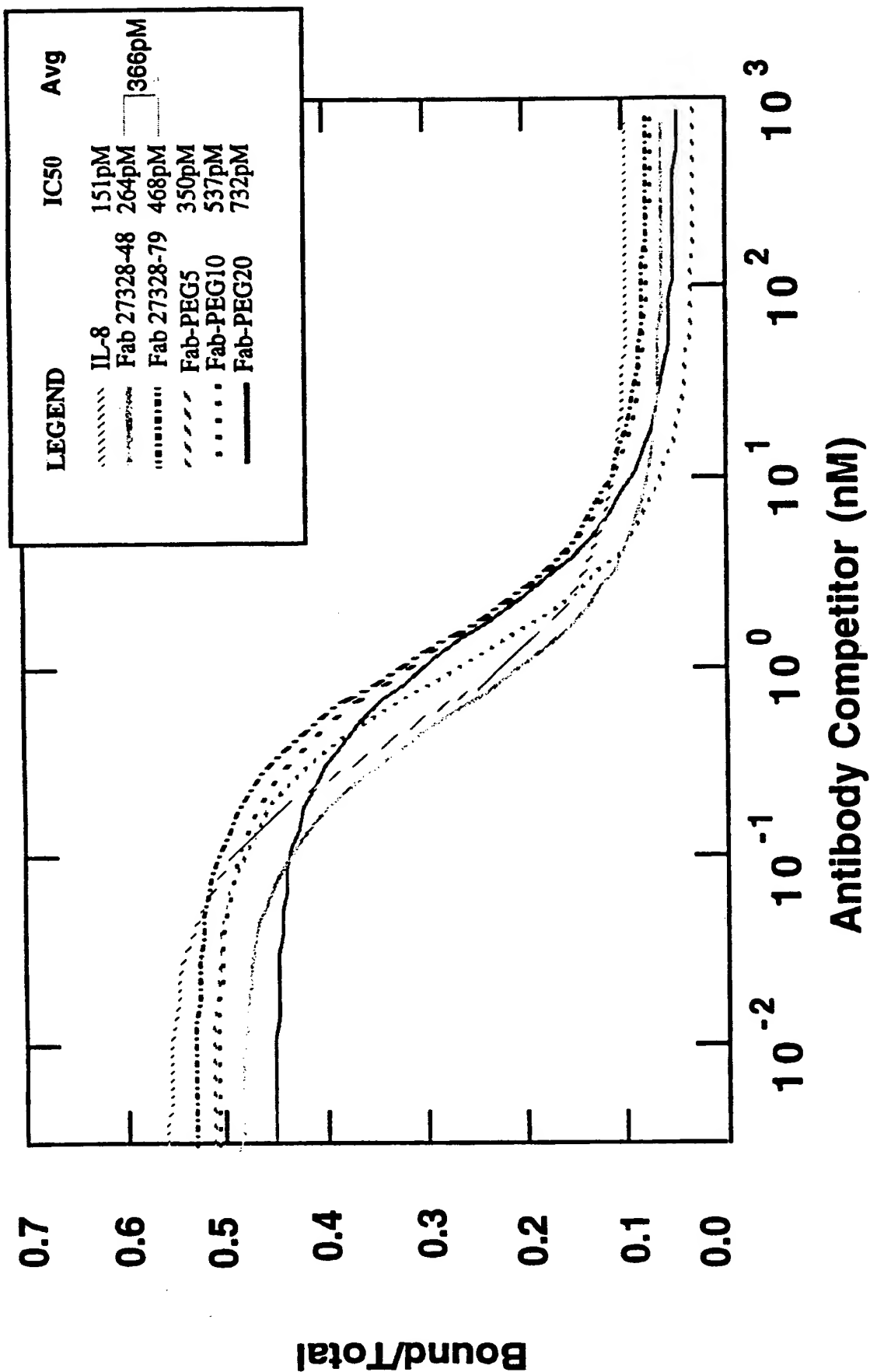


FIG. 54A

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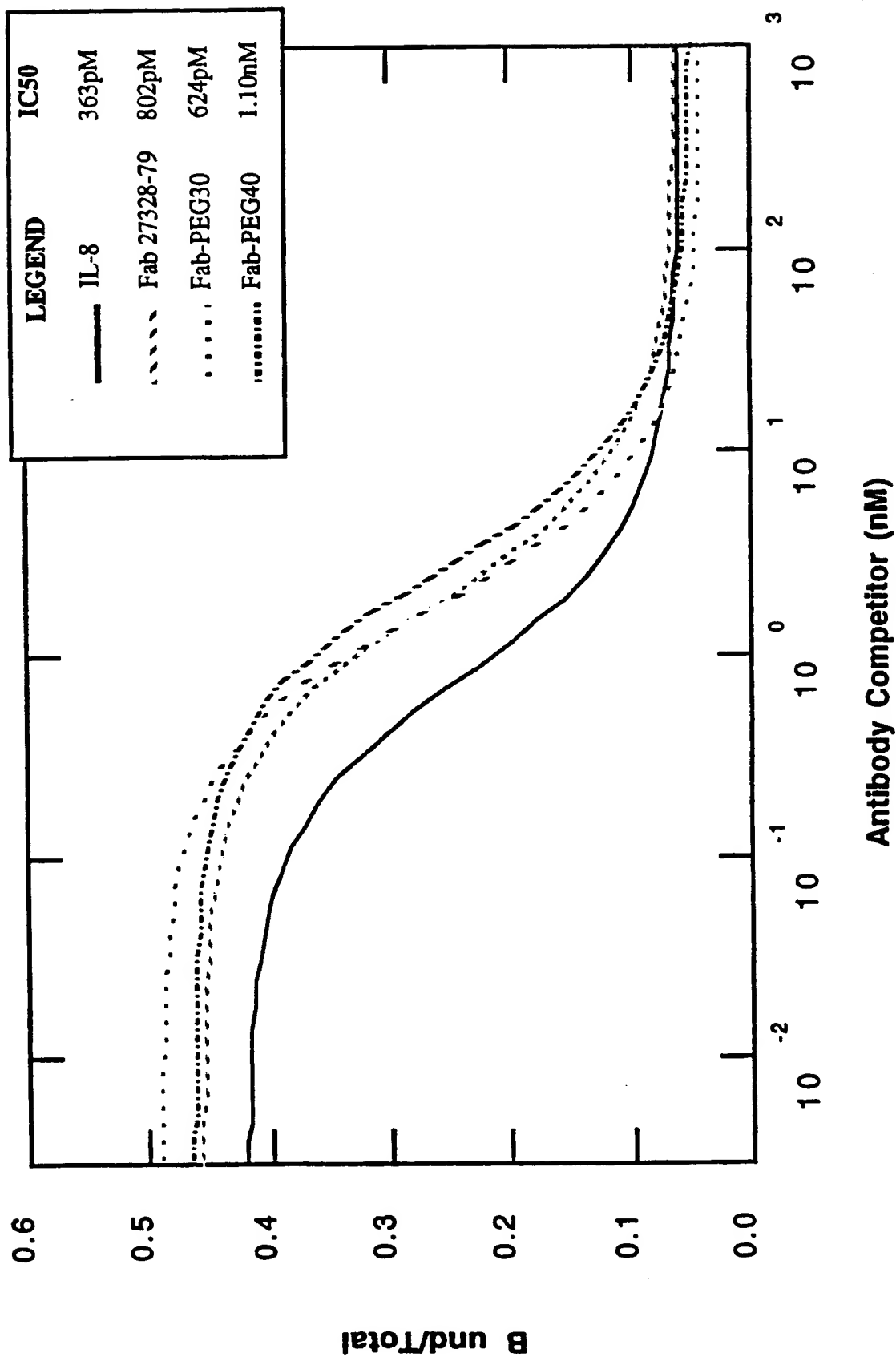
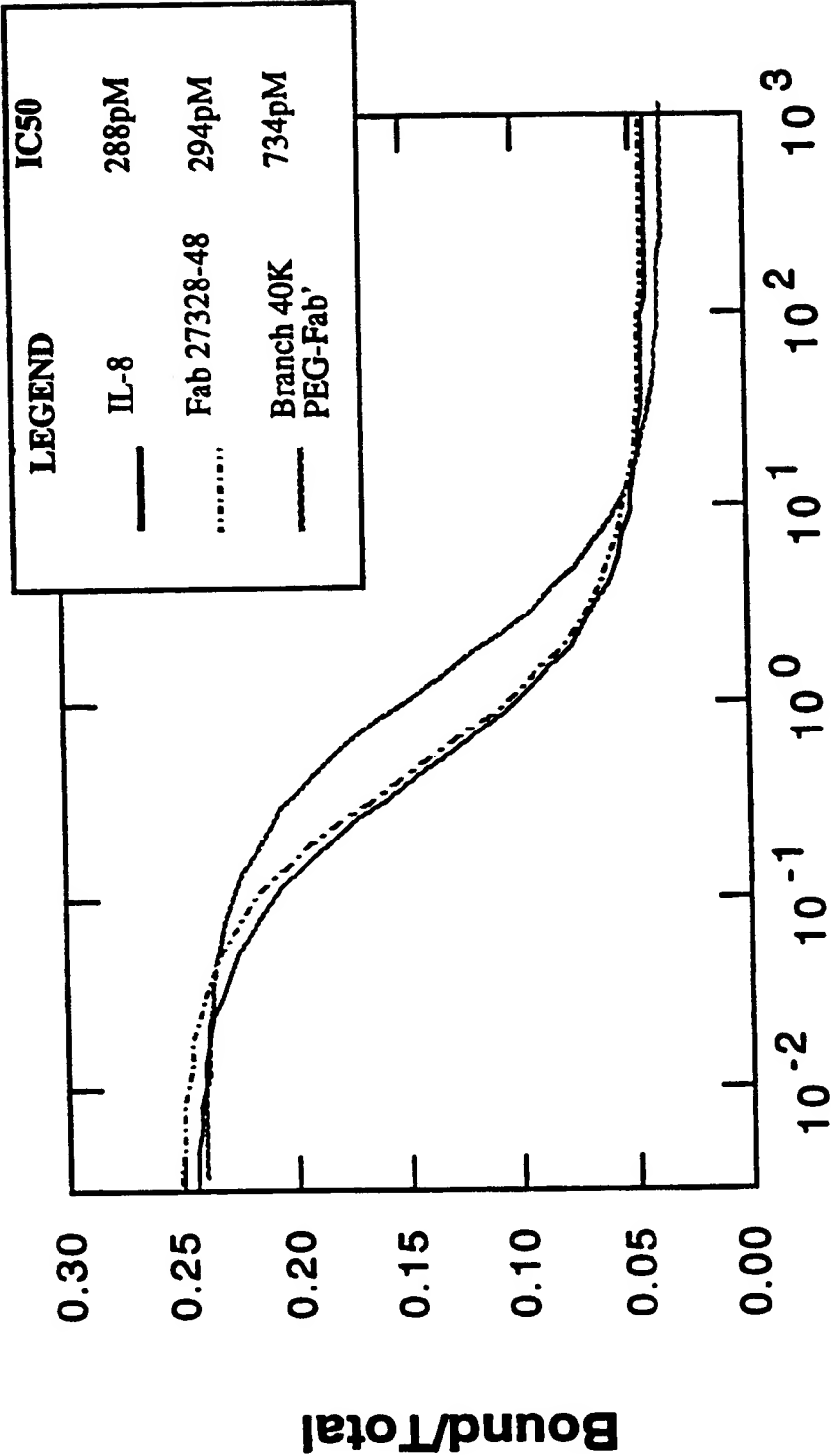


FIG. 54B



Antibody Competitor (nM)

FIG. 54C

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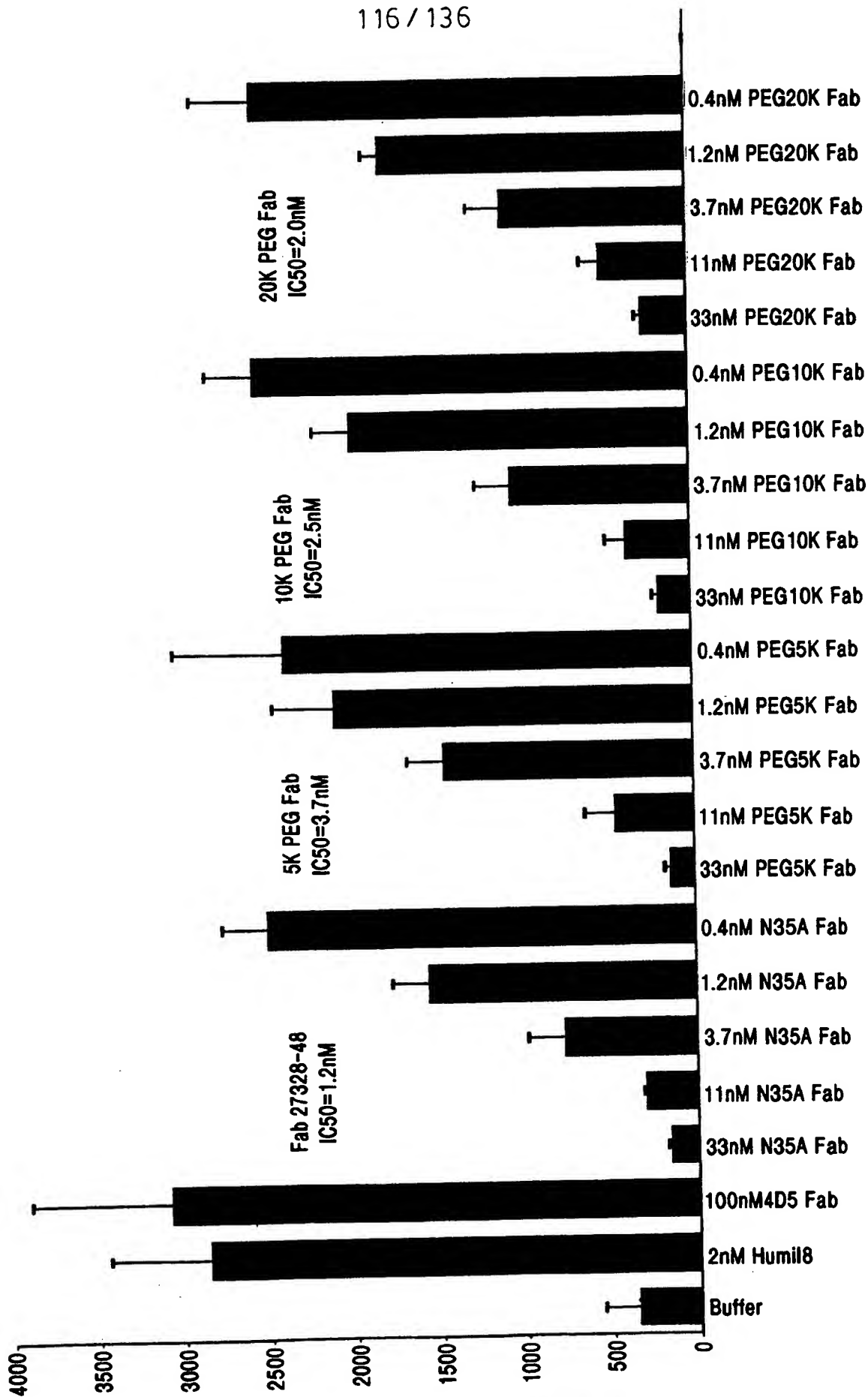


FIG. 55A

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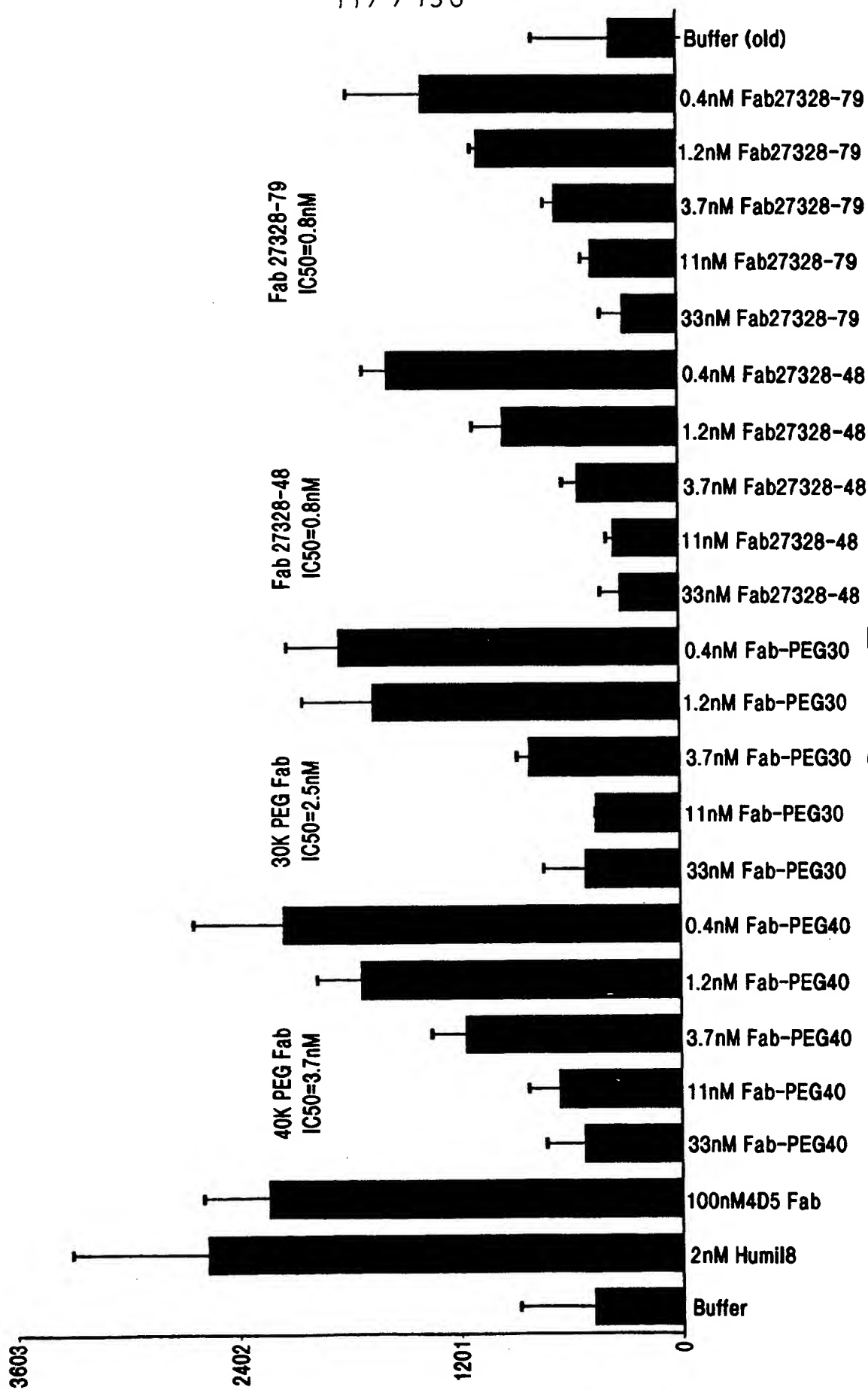


FIG. 55B

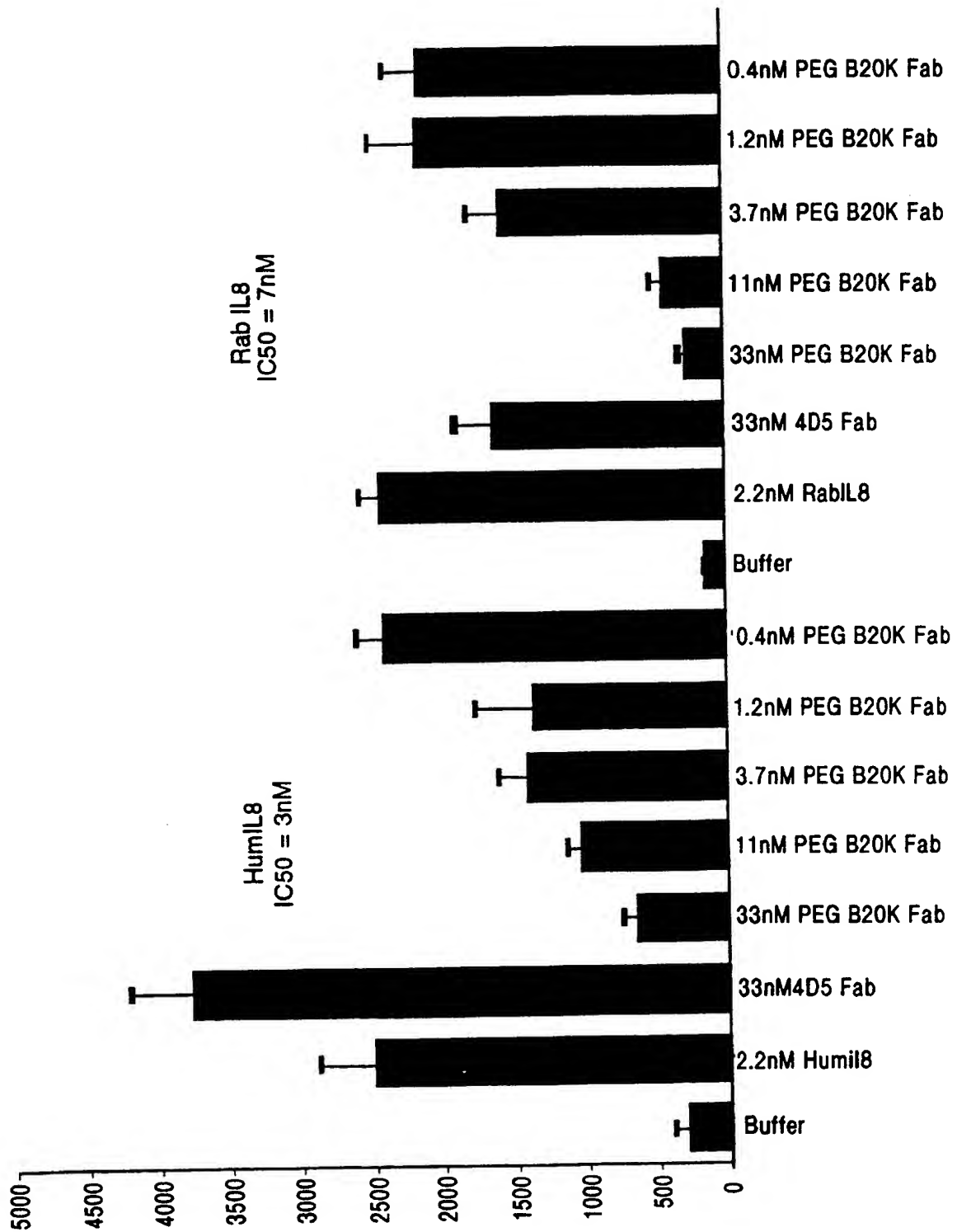
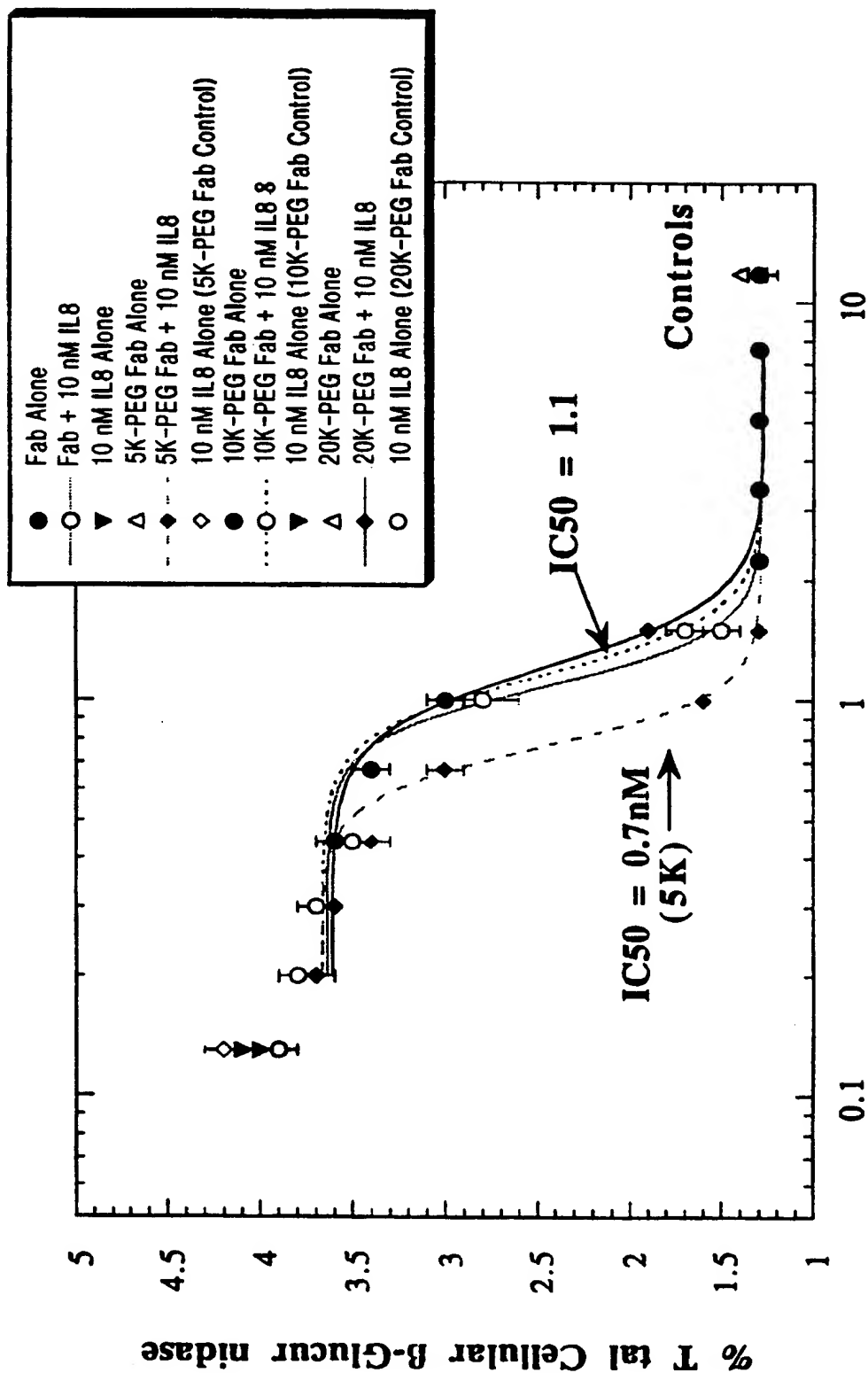


FIG. 55C



Molar Ratio Antibody:IL-8

FIG. 56A

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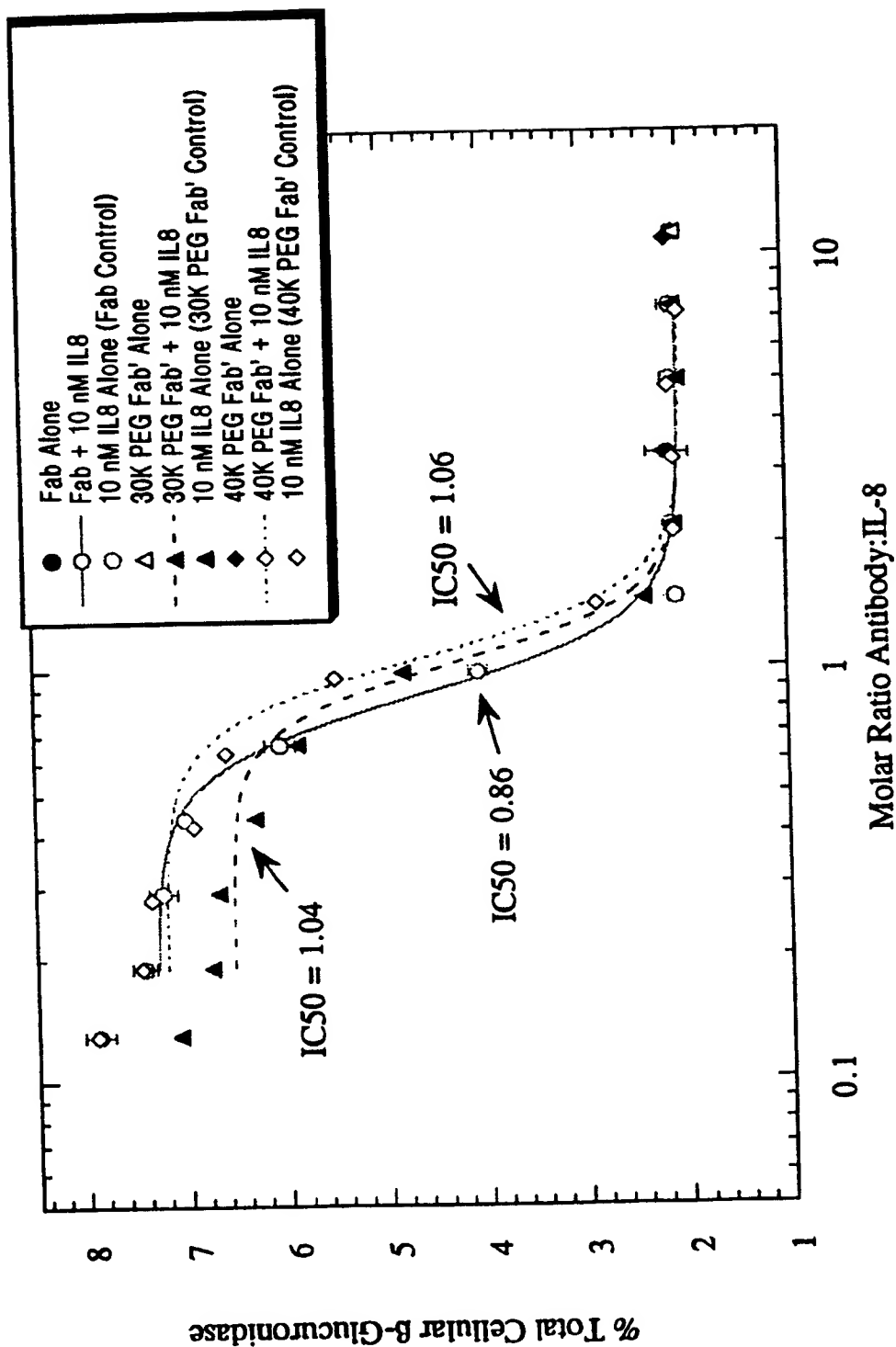
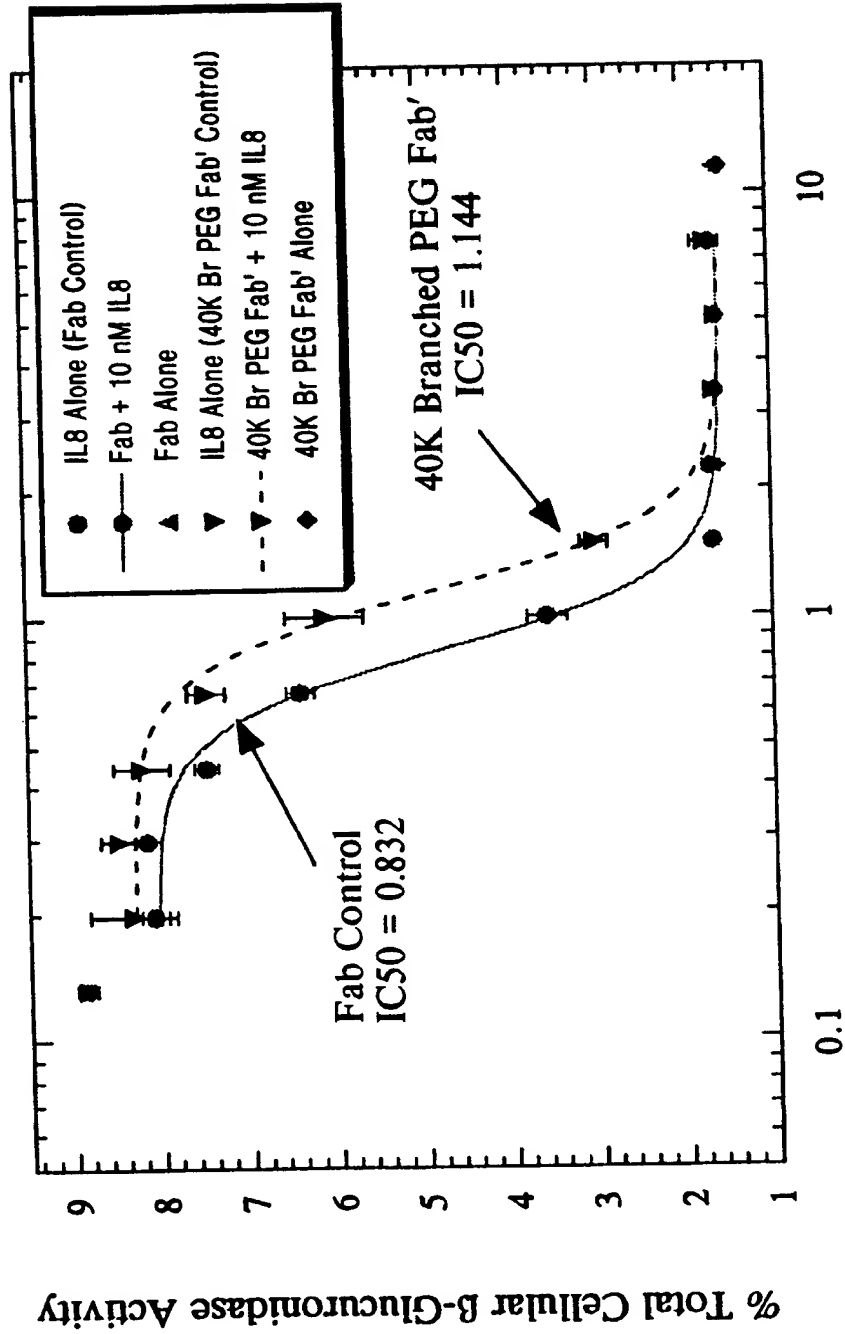


FIG. 56B

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Molar Ratio Antibody:IL8

FIG. 56C

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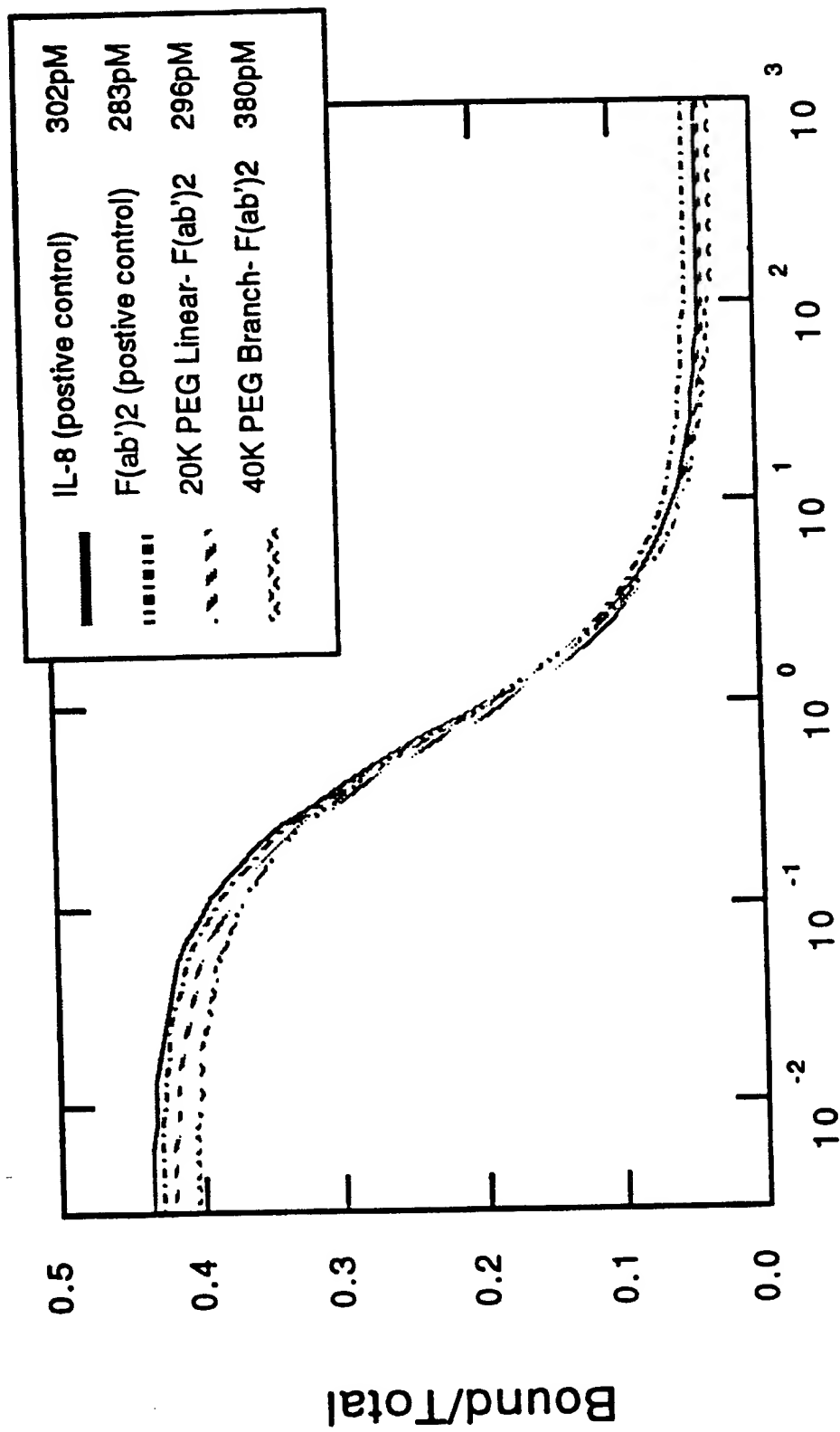
Pegylated F(ab')₂ (nM)

FIG. 57A

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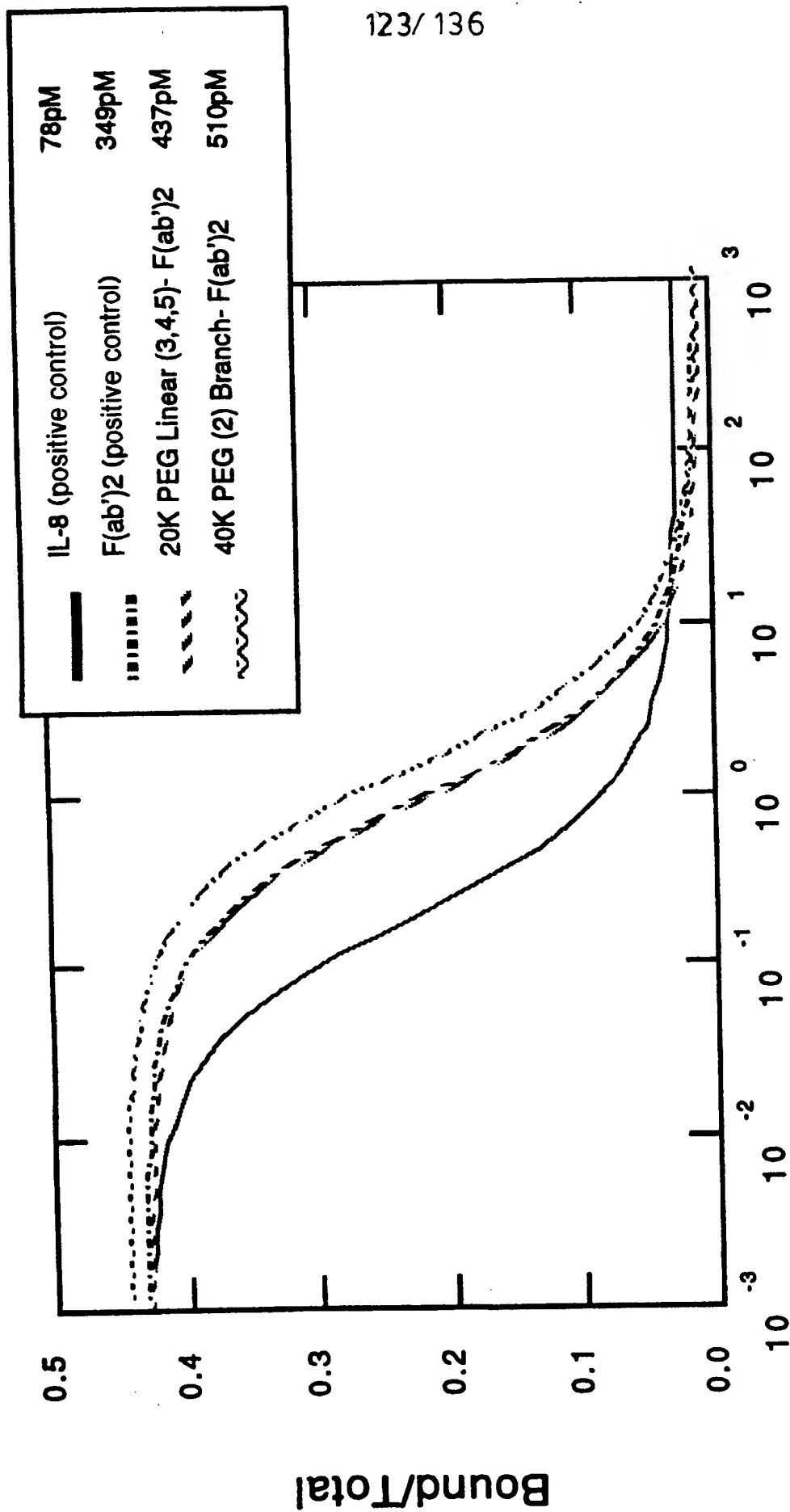
Pegylated F(ab')₂ (nM)

FIG. 57B

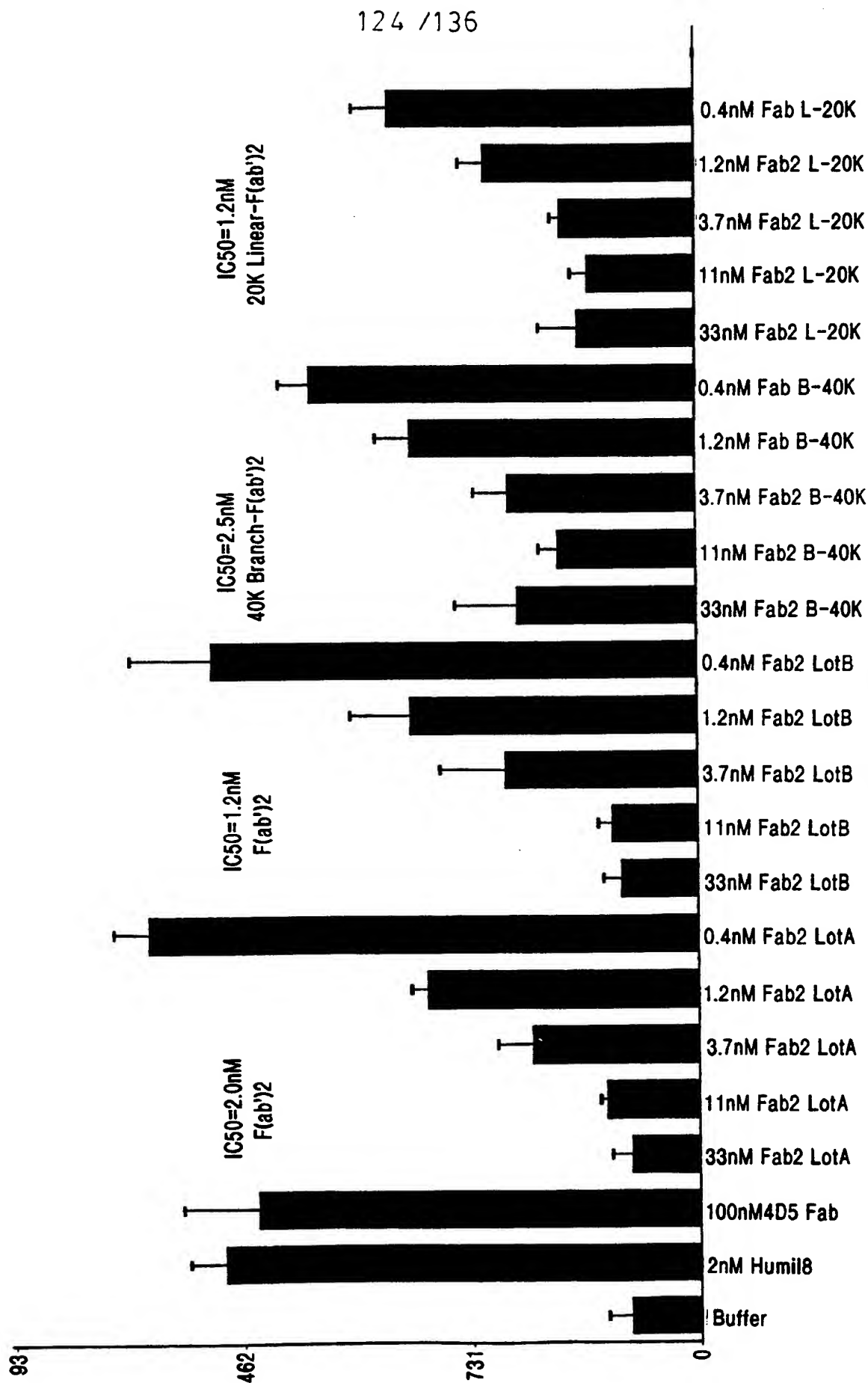


FIG. 58A

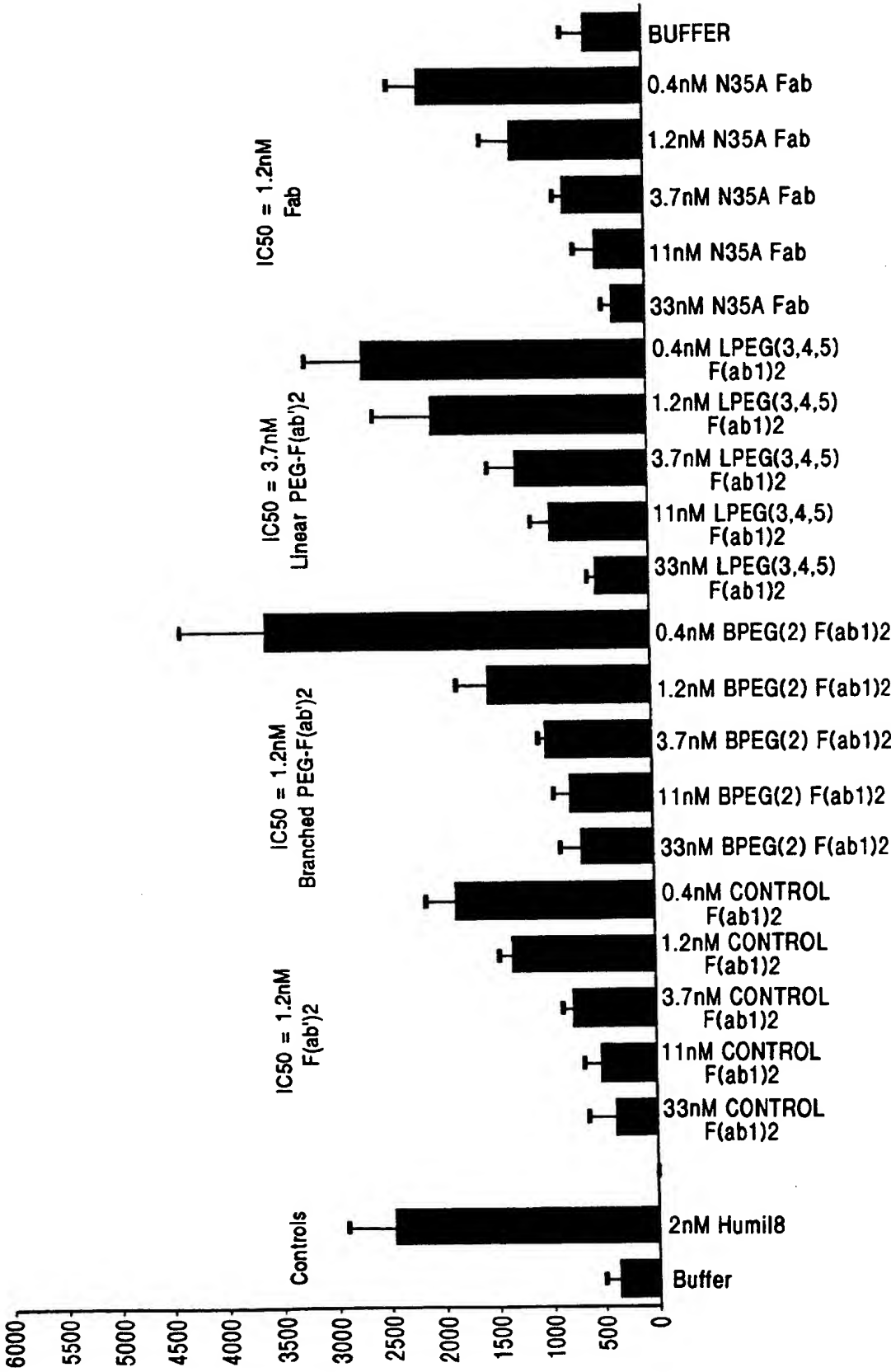
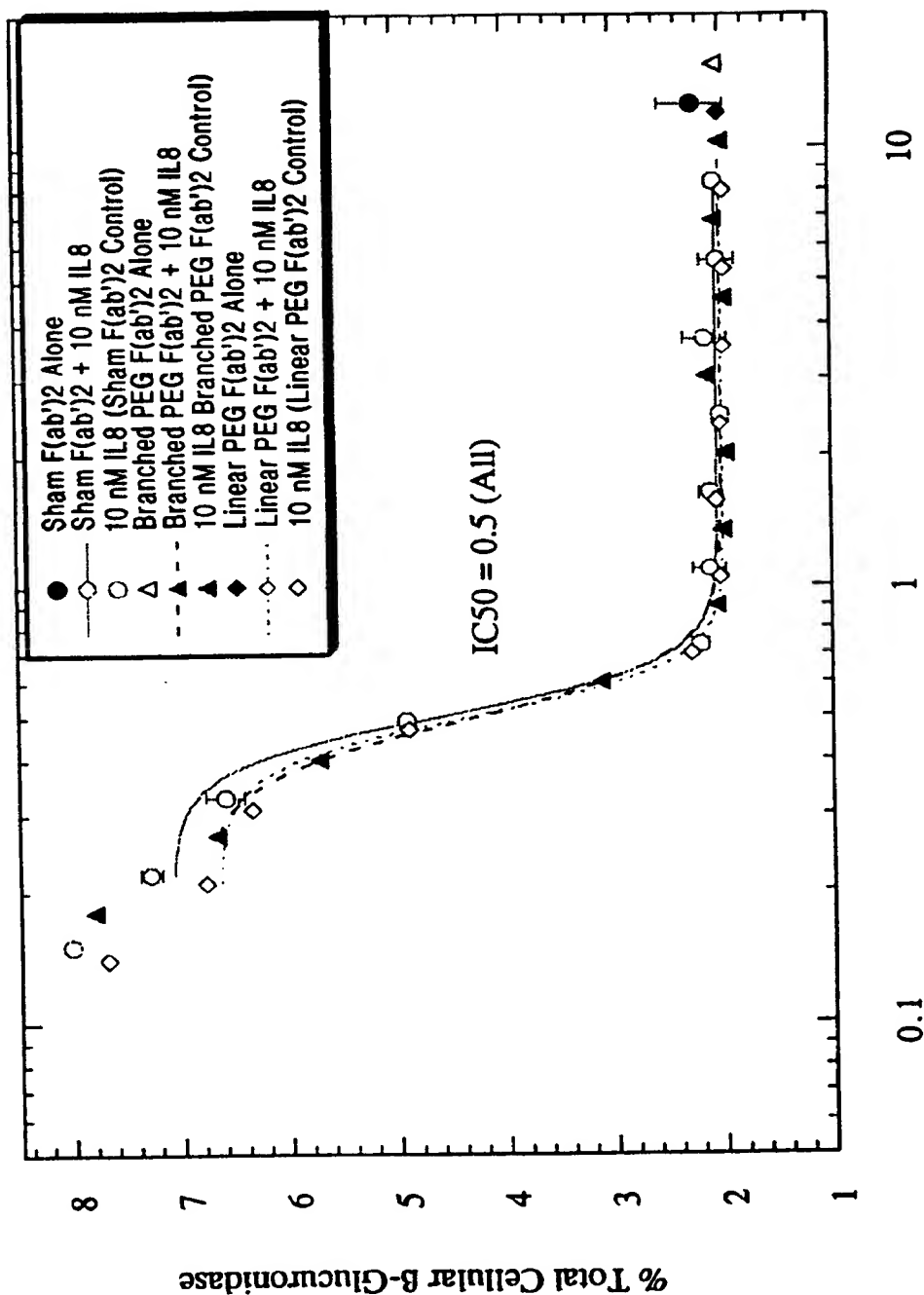


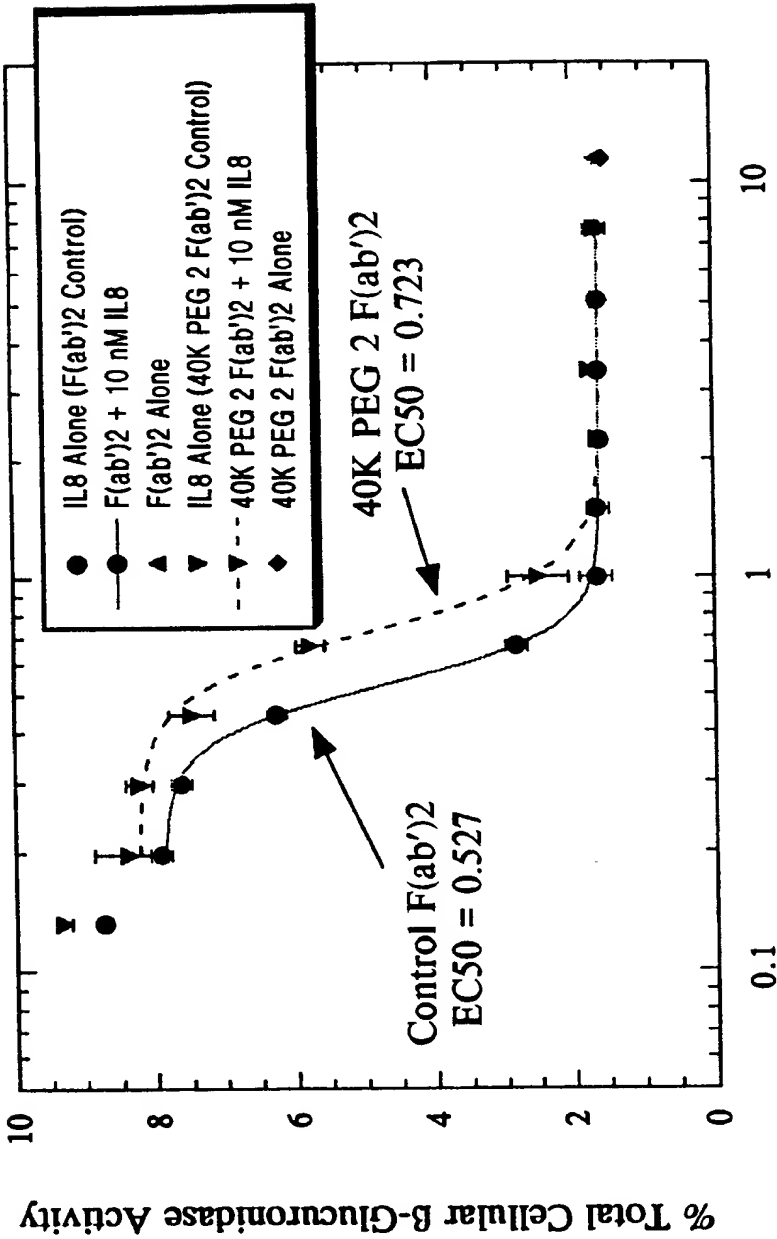
FIG. 58B

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Molar Ratio Antibody:IL-8

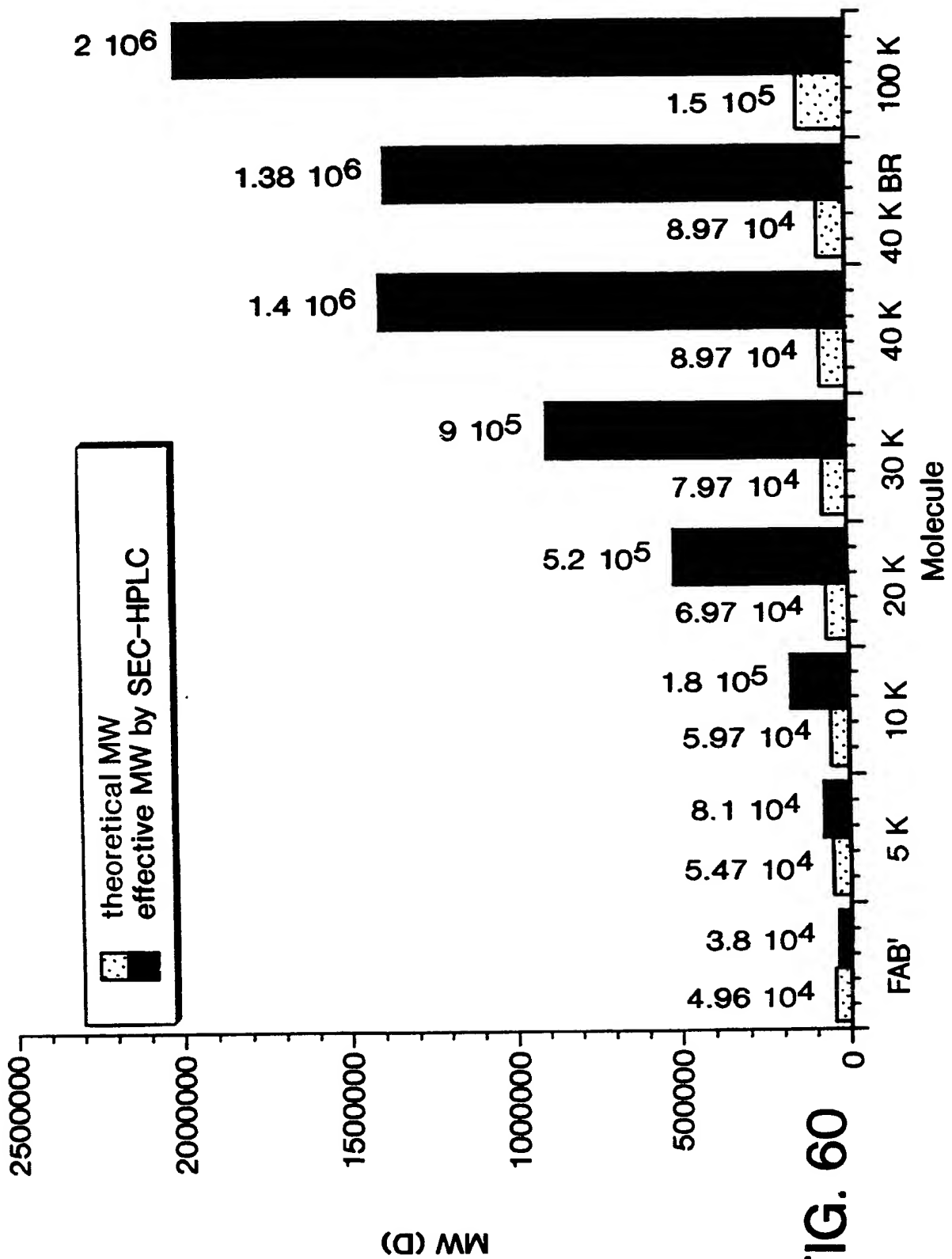
FIG. 59A

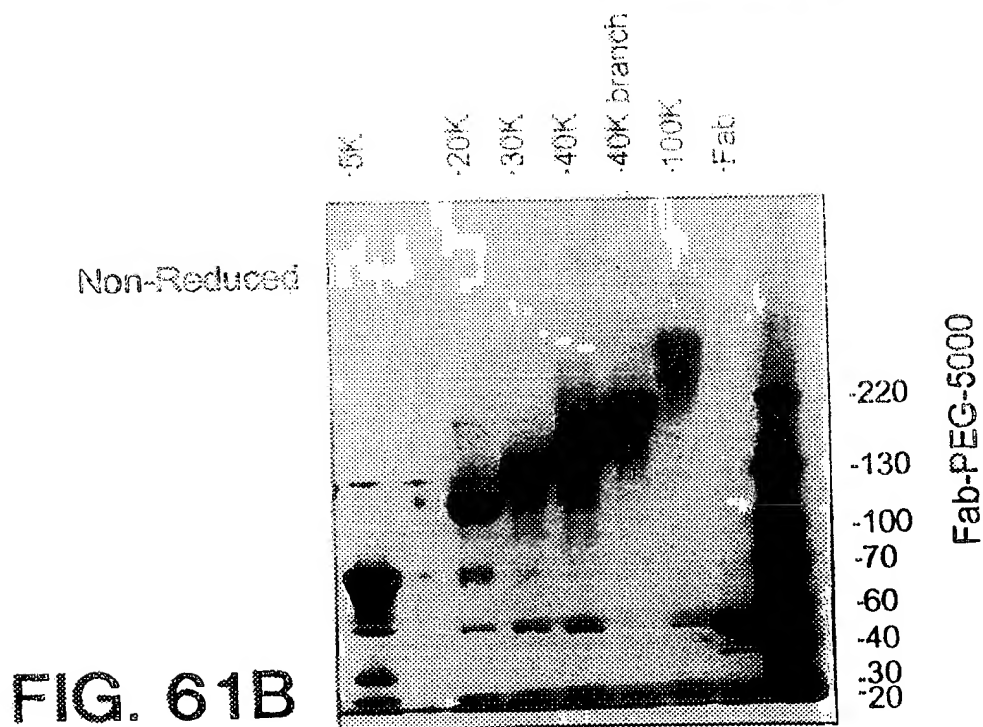
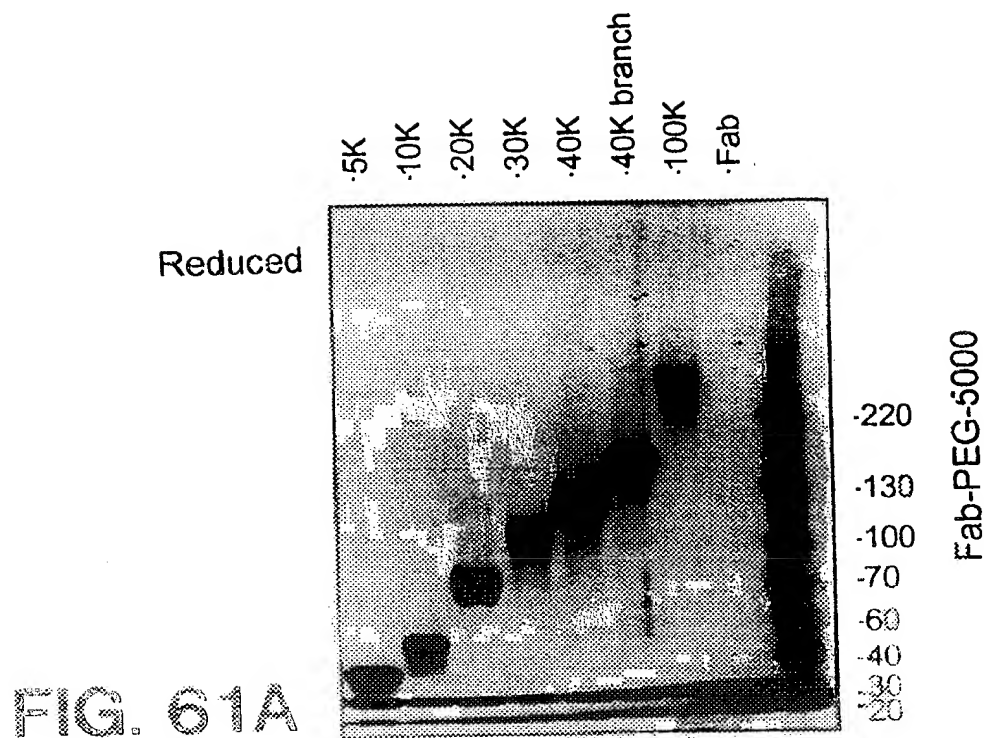


Molar Ratio Antibody:IL8

FIG. 59B

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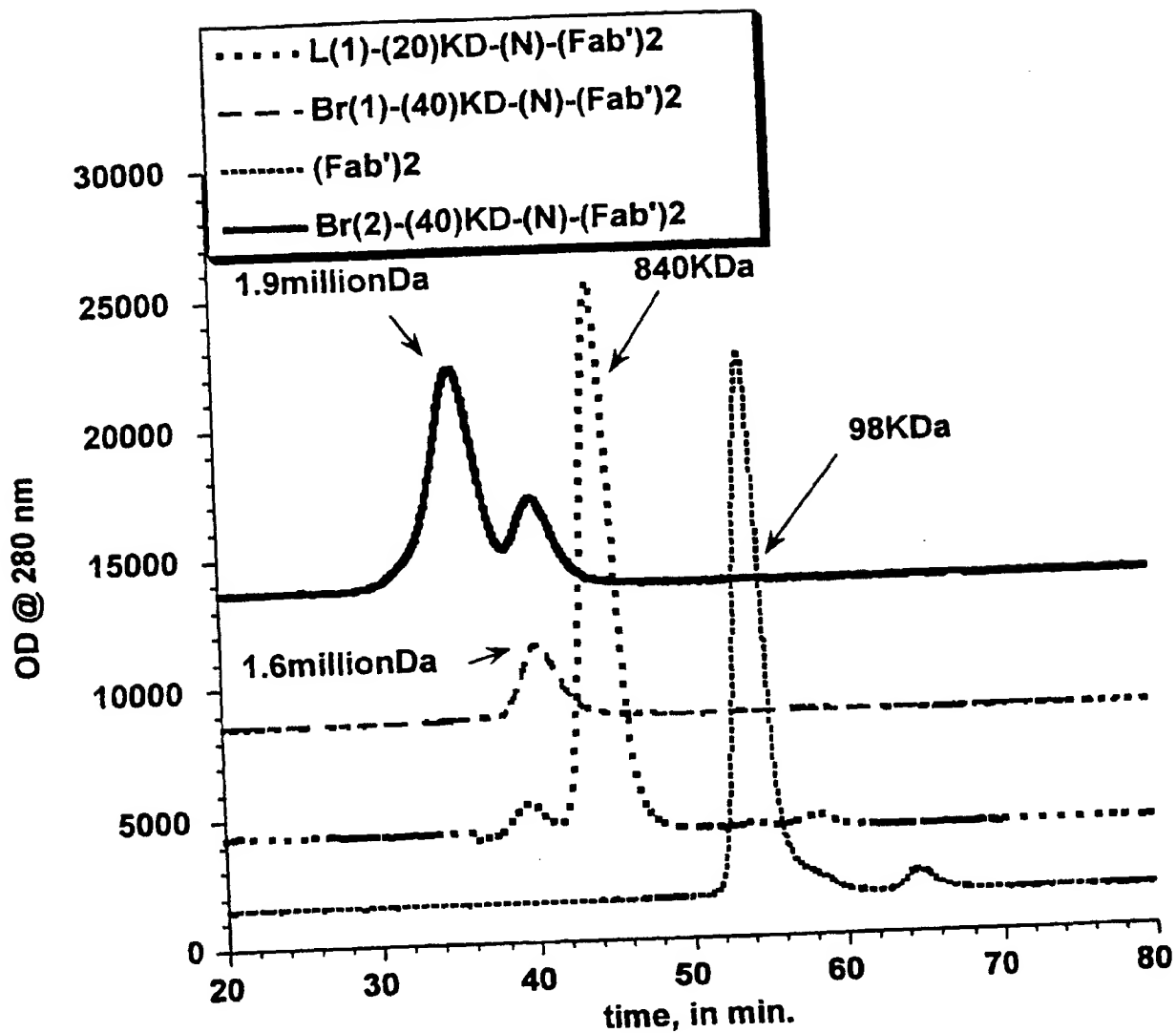


FIG. 62

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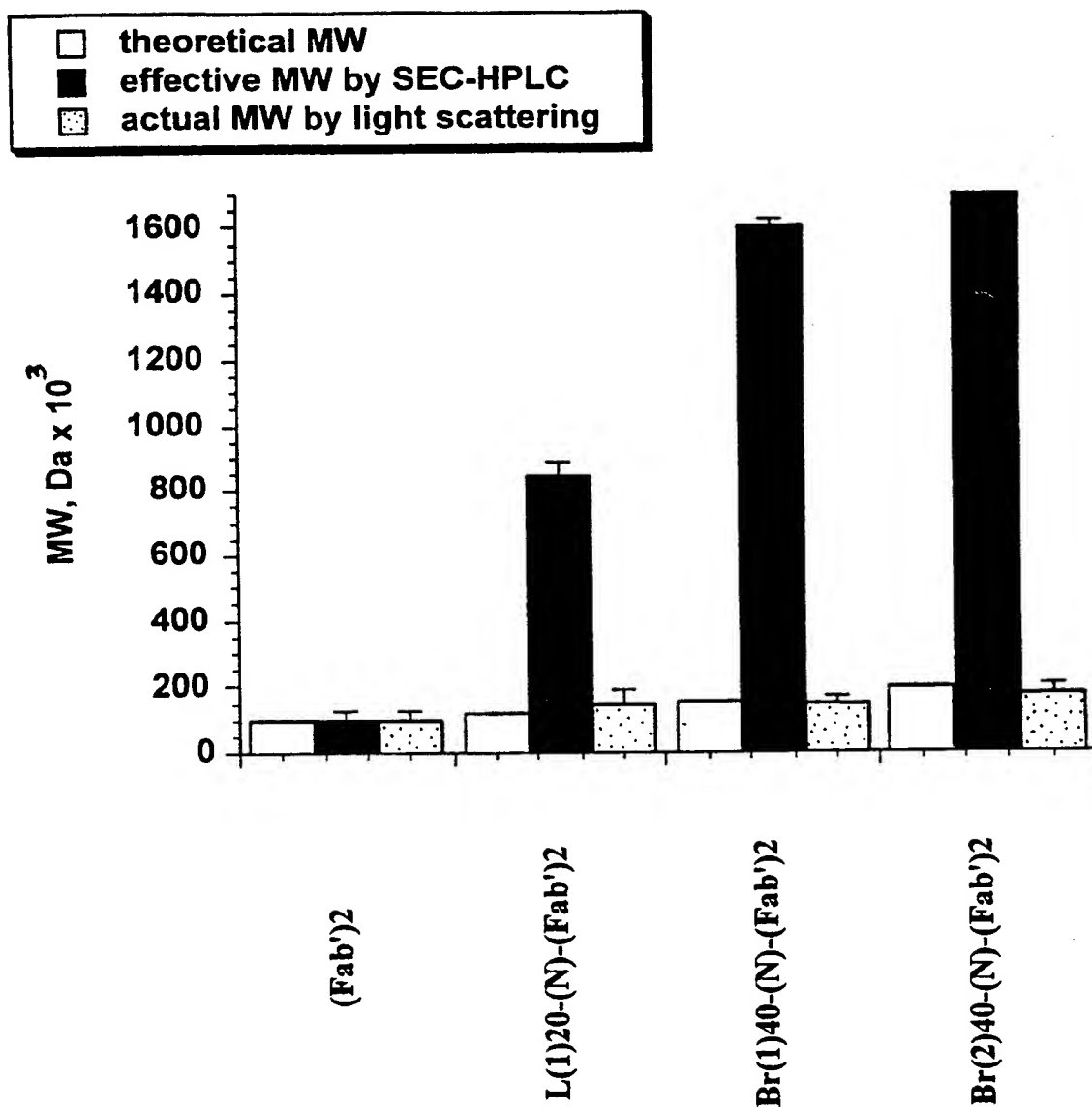


FIG. 63

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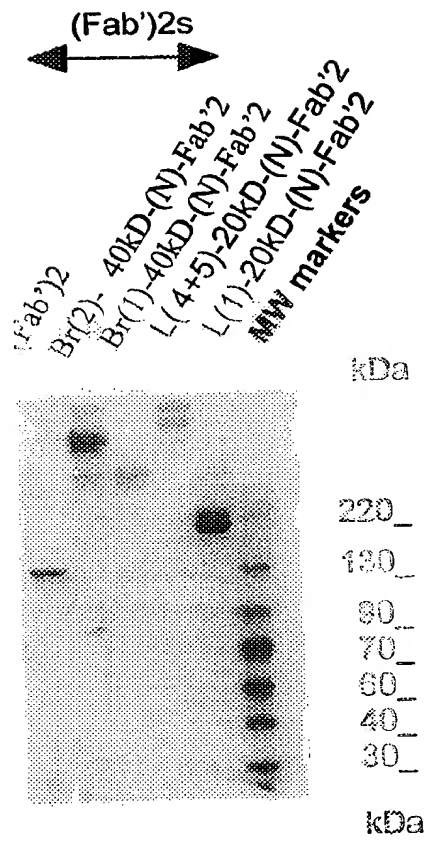
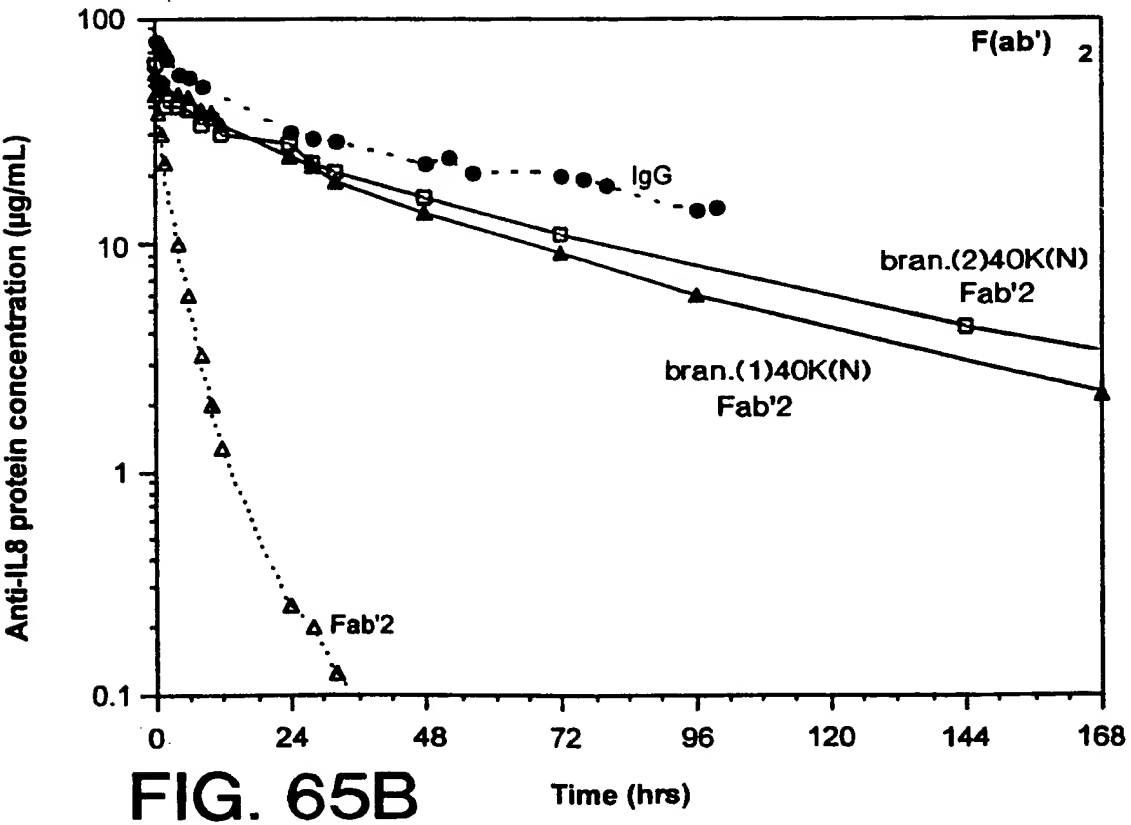
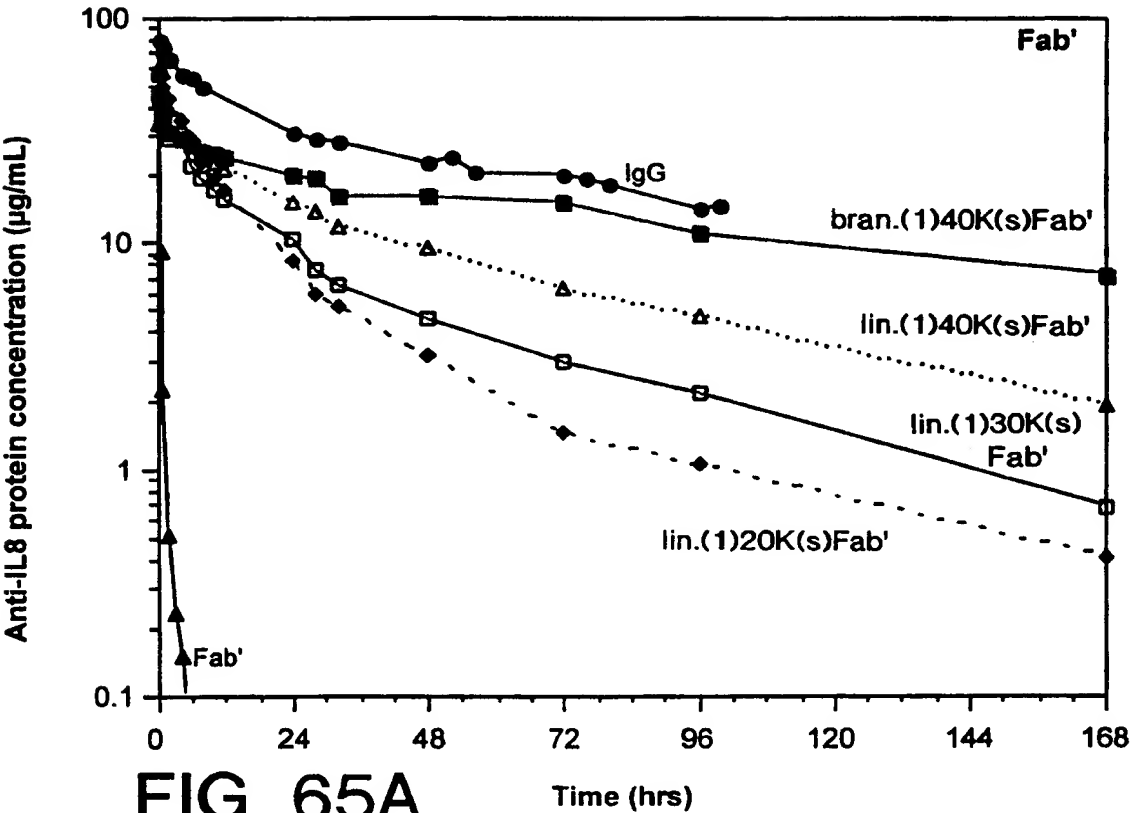


FIG. 64



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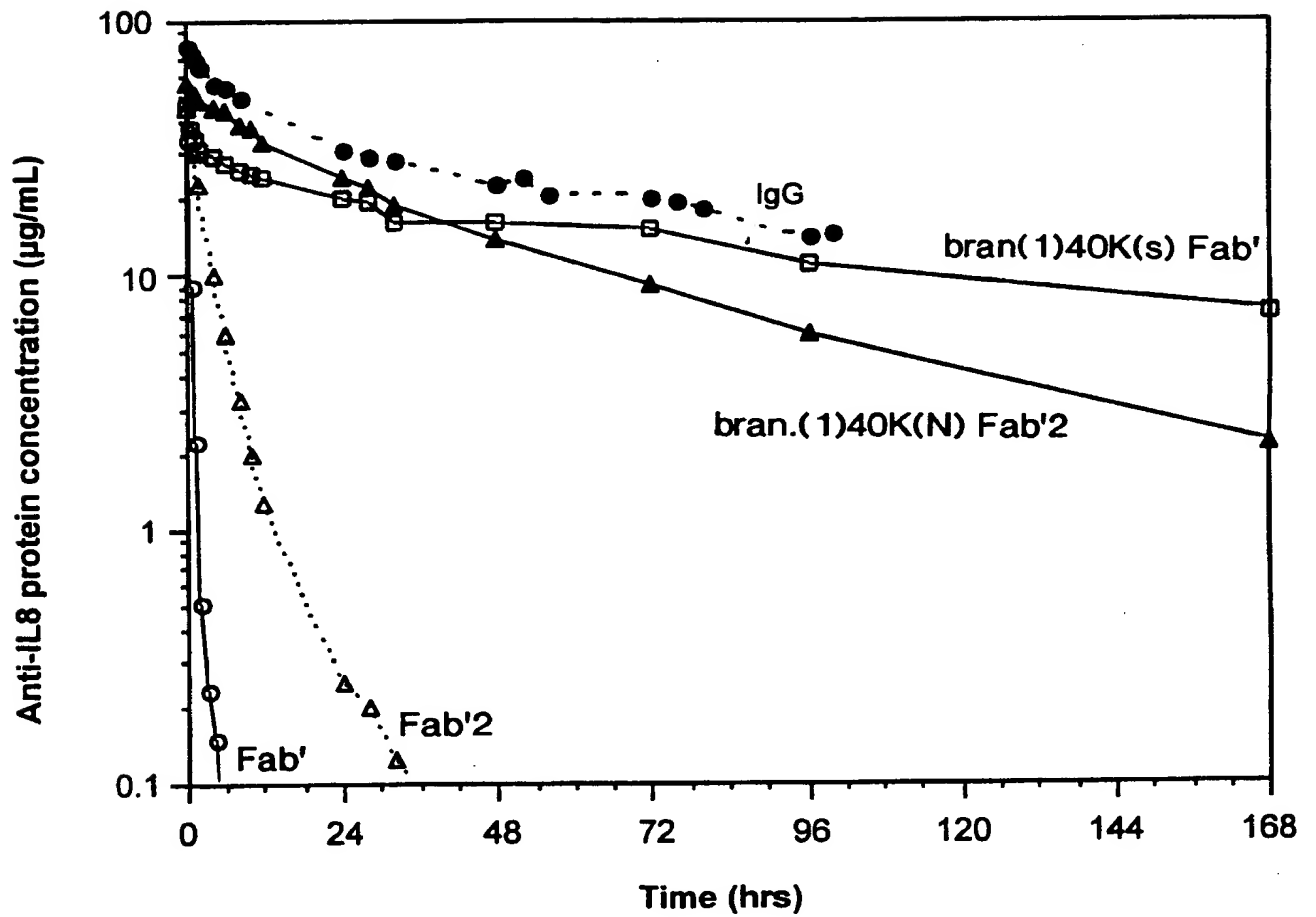


FIG. 66

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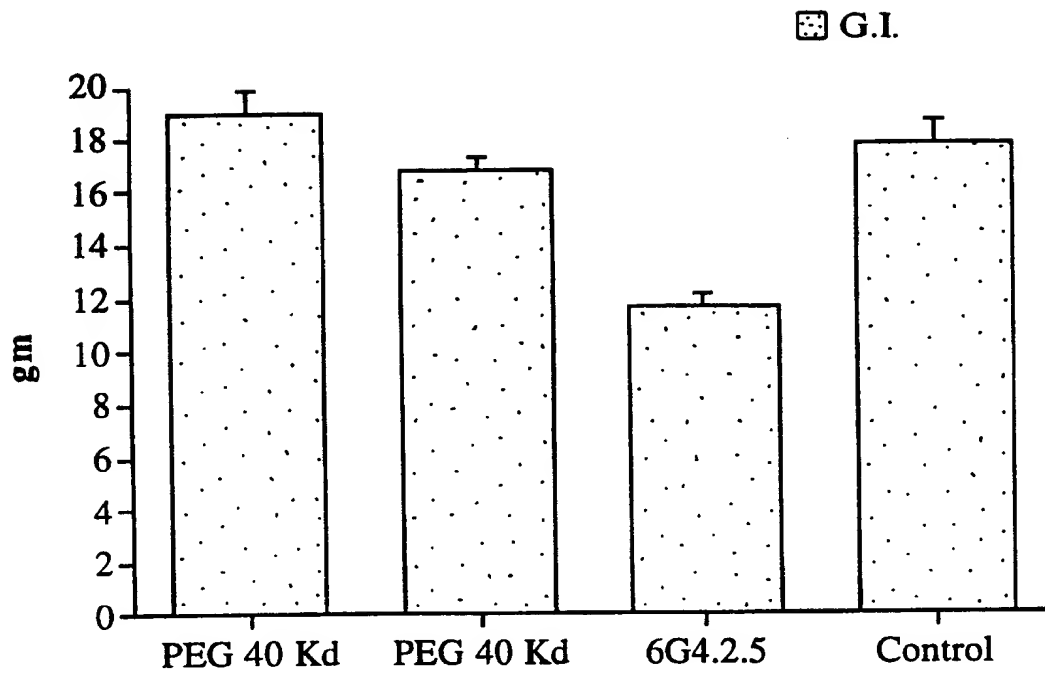


FIG. 67

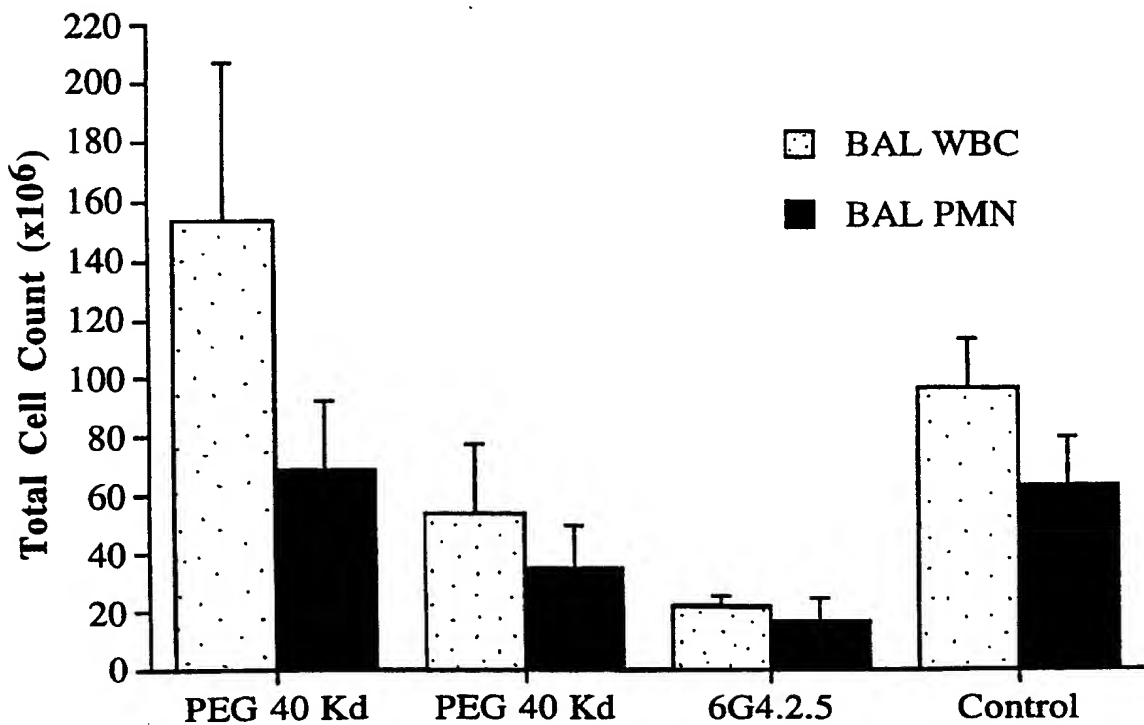


FIG. 68

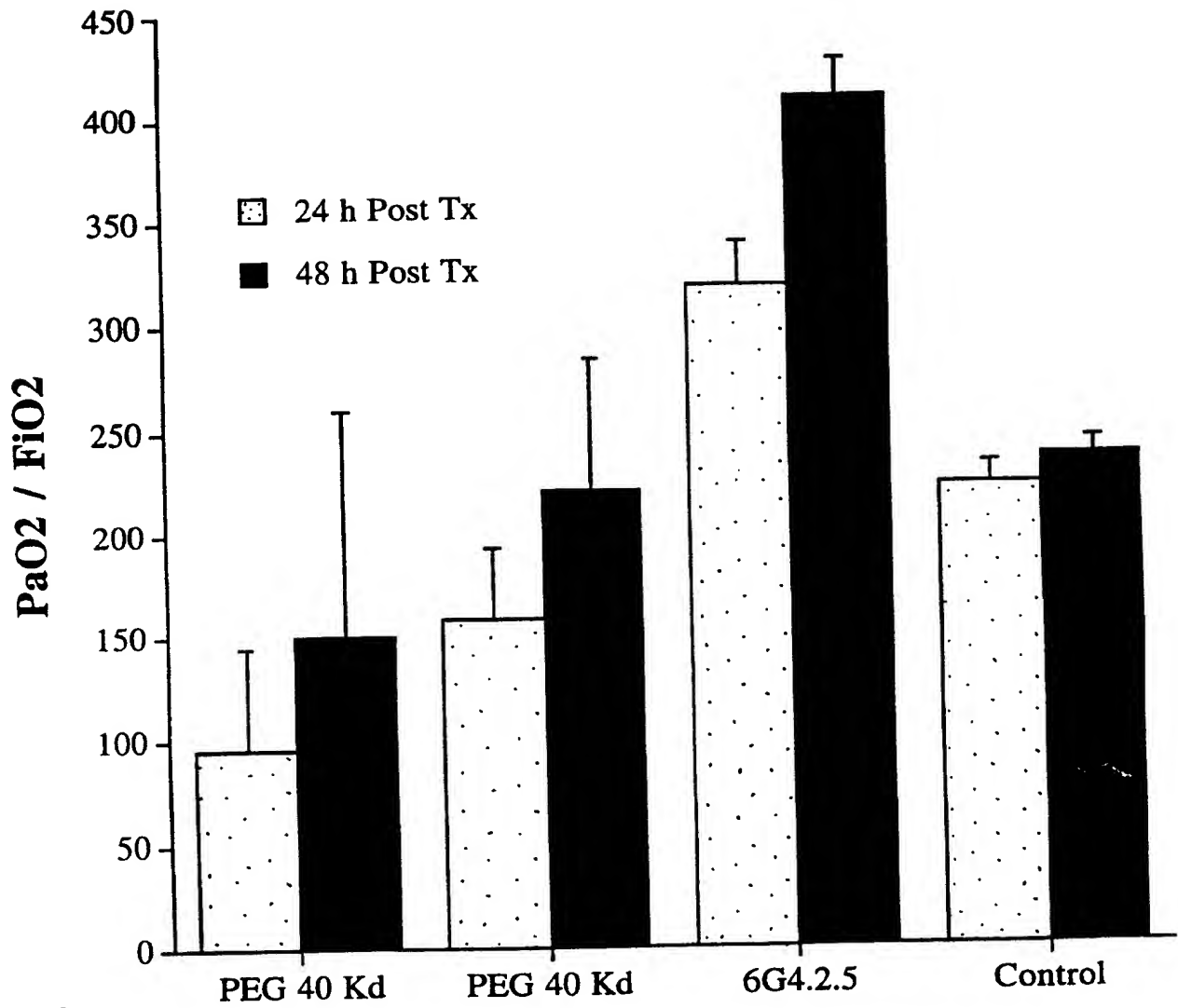


FIG. 69